LANE MEDICAL LIBRARY STANFORD
L961 .M289 1921 STOR
Manson's tropical diseases : a manual of
24503321840

Digitized by Google

LANE
MEDICAL LIBRARY

Gift
Library of Dr.Ernest S.du Bray

Digitized by Google

Digitized by Google

MANSON'S
TROPICAL DISEASES

Digitized by Google

Digitized by Google

MANSON'S TROPICAL DISEASES

A MANUAL OF THE DISEASES OF WARM CLIMATES

Ernest S. du Bray
Oct 5-1921
S.F.

EDITED BY

PHILIP H. MANSON-BAHR

D.S.O., M.A., M.D. (D.T.M. AND H.) CANTAB.,
M.R.C.P. LOND.

Physician to the Hospital for Tropical Diseases, London, and the Albert Dock Hospital; Lecturer at the London School of Tropical Medicine; Lecturer on Tropical Diseases at the North-East London Post-Graduate College; Examiner in Tropical Medicine to Cambridge University

Seventh Edition, Revised and Enlarged

WITH 21 COLOUR PLATES, 6 HALF-TONE PLATES,
404 FIGURES IN THE TEXT, AND 31 CHARTS

Dr. Ernest S. du Bray
1251 FLOOD BUILDING
SAN FRANCISCO

NEW YORK
WILLIAM WOOD AND COMPANY
1921

Digitized by Google

ALL RIGHTS RESERVED

Digitized by Google

L961
M49
1921

PREFACE TO THE SEVENTH EDITION

SINCE the publication of the Sixth Edition of this work, in 1917, many advances in Tropical Medicine have been made, and much that before was vague and hypothetical has become precise and been either confuted or confirmed. Much of this is attributable to experience in the Great War.

Outside the war zone scientific workers have not been idle. Noguchi and his fellow-countrymen have described a new group of parasites—the Leptospiræ, which are probably responsible for yellow fever, Weil's disease, and allied fevers of hitherto unknown etiology. They have been equally diligent and successful in elucidating other important problems, especially in helminthology.

Of recent years the subject of tropical fevers has greatly expanded, and it has been found necessary to devote twenty-three chapters of the Manual to this group of diseases. Recent additions to our knowledge of the enteric group have been incorporated in what is virtually a new chapter, for much of which I am indebted to Dr. R. P. Garrow.

In providing for these and other subjects, it has been necessary to rearrange and rewrite a considerable portion of the book, and to find room for a mass of technical detail in a series of Appendices devoted to Protozoology, Medical Zoology, and Laboratory Methods. Though they are not intended to take the place of more exhaustive treatises on these subjects, I feel that the inclusion of

Digitized by Google

these Appendices will be of service to the student, and especially to the isolated worker in the Tropics.

In order to render them complete, I have not scrupled to repeat, or to amplify, facts already set out in the text, so that those who use the Appendices may find in them all the information they require.

Major Austen, D.S.O., has kindly revised the section dealing with Tse-tse Flies.

In threading the mazes of Medical Protozoology I have benefited by the advice of Professor Clifford Dobell, F.R.S.

Dr. Andrew Balfour, C.B., C.M.G., and his associates at the Wellcome Bureau of Scientific Research have afforded assistance on many difficult points.

From my colleagues at the London School of Tropical Medicine I have received similar sympathetic help.

I desire also to acknowledge the loyal and devoted help of my former assistants, Mr. W. J. Muggleton and Mr. T. R. Goddard, in the preparation of the Laboratory Appendix. To the latter gentleman I am to a great extent indebted for a description of a method of performing the Wassermann reaction suitable for the Tropics.

A large number of new Plates and Figures in the text have been added. To Dr. J. Gordon Thomson I am indebted for the fine colour drawing illustrating the Malaria Parasites (Plate I.). The originals of Plates II., IV., V. were painted by Dr. J. K. Lund, who has been good enough to place his artistic skill at my service. Dr. John Bell has kindly supplied a number of valuable microphotographs.

To Dr. Eric Bellingham-Smith I am indebted for a selection of typical temperature charts.

Digitized by Google

Special acknowledgment must be made to Professor Brumpt, to Professor Nuttall, F.R.S., to the Editors of the *Journal of Experimental Medicine*, to the Editors of the *Journal of Parasitology*, and to the Trustees of the British Museum and of the Rockefeller Foundation, for permission to adapt or otherwise make use of illustrations that have appeared in their publications.

These acknowledgments would be incomplete without special reference to Dr. A. G. Bagshawe, the Editor of the *Tropical Diseases Bulletin*; but for the aid of that publication my task would have been impossible.

I have felt it a great honour that the charge of this famous Manual should have been entrusted to me. It is difficult for me to express adequately the debt I owe to the original author, Sir Patrick Manson, who has given freely of his ripe experience in revising proofs and making many valuable suggestions.

Dr. John Anderson has kindly read through the final proofs.

To prevent the work from becoming unduly bulky, the Publishers have enlarged the page and the type has been entirely reset. It is a pleasure to acknowledge their unfailing courtesy and helpfulness.

PHILIP MANSON-BAHR.

Weymouth Street, W.
January, 1921.

Digitized by Google

Digitized by Google

PREFACE TO THE FIRST EDITION

A MANUAL on the diseases of warm climates, of handy size, and yet giving adequate information, has long been a want; for the exigencies of travel and of tropical life are, as a rule, incompatible with big volumes and large libraries. This is the reason for the present work.

While it is hoped that the book may prove of practical service, it makes no pretension to being anything more than an introduction to the important department of medicine of which it treats; in no sense is it put forward as a complete treatise, or as being in this respect comparable to the more elaborate works by Davidson, Scheube, Rho, Laveran, Corre, Roux, and other systematic writers in the same field.

The author avails himself of this opportunity to acknowledge the valuable assistance he has received, in revising the text, from Dr. L. Westenra Sambon and Mr. David Rees, M.R.C.S., L.R.C.P., Superintendent, London School of Tropical Medicine. He would also acknowledge his great obligation to Mr. Richard Muir, Pathological Laboratory, Edinburgh University, for his care and skill in preparing the illustrations.

Digitized by Google

Digitized by Google

CONTENTS

Section I.—Fevers

CHAPTER		PAGE
1.	Malaria	1
2.	Description of the Various Species of Malaria Parasites and their Associated Fevers	27
3.	Epidemiology and Endemiology of Malaria	56
4.	Diagnosis, Treatment, and Prophylaxis of Malaria	62
5.	Malaria and the Mosquito	83
6.	Blackwater Fever	96
7.	Trypanosomiasis of Man	111
8.	Leishmaniasis	147
9.	Relapsing Fever	170
10.	Yellow Fever	190
11.	Infectious Jaundice	211
12.	Rat-bite Fever	217
13.	Seven-day Fever	219
14.	Dengue	221
15.	Phlebotomus Fever	230
16.	Spotted Fever of the Rocky Mountains	235
17.	Japanese River Fever	241
18.	Typhus Fever in the Tropics	246
19.	Plague	252
20.	Undulant Fever	278
21.	Enteric and Enteric-like Fevers in the Tropics	291
22.	Heat-stroke	316
23.	The Diagnosis of Fevers in the Tropics	327

Digitized by Google

Section II.—General Diseases of Undetermined Nature

CHAPTER		PAGE
24.	Beriberi	338
25.	Epidemic Dropsy (War Œdema)	361
26.	Pellagra	364
27.	Scurvy in the Tropics	377

Section III.—Abdominal Diseases

28.	Cholera	380
29.	The Dysenteries	404
30.	The Dysenteries (*concluded*)	430
31.	Sprue (Psilosis)	473
32.	Hill Diarrhœa	490
33.	Tropical Liver	492
34.	Infantile Biliary Cirrhosis	496
35.	Egyptian Splenomegaly	498

Section IV.—Infective Granulomatous Diseases

36.	Leprosy (Elephantiasis Græcorum)	501
37.	Yaws (Frambœsia)	526
38.	Oroya Fever and Verruga Peruviana	541
39.	Ulcerating Granuloma of the Pudenda	548

Section V.—Animal Parasites and Associated Diseases

40.	Parasites of the Circulatory System: Schistosomiasis	553
41.	Parasites of the Lymphatic System and Connective Tissues: Filariasis	581
42.	Parasites of the Lymphatic System and Connective Tissues: Filariasis (*concluded*)	631
43.	Parasites of the Lung and Liver: Paragonimiasis; Clonorchiasis	647
44.	Intestinal Parasites	653

Digitized by Google

Section VI.—Diseases due to Poisons, including Snake-bite

CHAPTER PAGE
45. Vegetable Poisons 679
46. Animal Poisons 684

Section VII.—Tropical Skin Diseases

47. Non-specific, Bacterial, Fungous Diseases, etc. . 693

Section VIII.—Local Diseases of Uncertain Nature

48. Craw-craw — Chappa — Climatic Bubo—Goundou — Ainhum—Big Heel—Onyalai 738

Appendix I.—Medical Protozoology

Sarcodina 749
Mastigophora 755
Sporozoa 770
Ciliophora 782
Spirochætes 782

Appendix II.—Medical Helminthology, Entomology, etc.

Phylum Platyhelminthes 784
The Trematoda 784
The Cestoda 804
Phylum Nemathelminthes 819
The Nematoda 819
The Gordiaciæ 849
The Acanthocephala 850
Phylum Annelida 851
Phylum Arthropoda 852
The Arachnida 853
The Insecta 863

Digitized by Google

PAGE

CLASSIFICATION OF SNAKES (ORDER OPHIDIA) . . 872
COLUBRIDÆ 873
VIPERIDÆ 874

Appendix III.—Laboratory Methods as applied to Clinical Medicine in the Tropics

1. CLEANING SLIDES AND COVER-SLIPS 878
2. METHODS OF PREPARATION OF BLOOD-FILMS . . 878
3. STAINING OF BLOOD-FILMS FOR PROTOZOA AND FOR THE DIFFERENTIAL COUNT OF CELLS 881
4. MEASUREMENT OF MICROSCOPIC OBJECTS . . . 884
5. VARIETIES OF BLOOD-CELLS, AND THEIR SIGNIFICANCE . 885
6. ENUMERATION OF BLOOD-CELLS AND ESTIMATION OF HÆMOGLOBIN 887
7. PREPARATION OF USEFUL CULTURE MEDIA . . . 888
8. CULTIVATION OF PROTOZOA AND BACTERIA FROM THE BLOOD, CEREBRO-SPINAL FLUID, ETC. 895
9. AGGLUTINATION WITH PATIENT'S SERUM FOR TYPHOID, PARATYPHOID, AND WEIL-FELIX REACTION . . 897
10. RECOGNITION OF ORGANISMS ISOLATED FROM THE FÆCES AND URINE BY AGGLUTINATION . . 902
11. CHEMICAL AND MICROSCOPICAL EXAMINATION OF FÆCES 903
12. EXAMINATION OF URINE IN THE TROPICS . . . 908
13. SPECTROSCOPIC EXAMINATION OF URINE AND OTHER FLUIDS 909
14. DETECTION OF SPIROCHÆTES, SPIRONEMES, AND THE GONOCOCCUS 910
15. A PRACTICAL METHOD OF PERFORMING THE WASSERMANN REACTION, SUITABLE FOR THE TROPICS . 913
16. FIXATION OF TISSUES FOR PARAFFIN SECTIONS . . 920
17. PRESERVATION OF TISSUES FOR MUSEUM PURPOSES . 924
18. REARING, DISSECTING, AND PRESERVING MOSQUITOES . 925
19. FORMULÆ OF STAINS COMMONLY IN USE . . . 928
20. SCALES AND STANDARDS 931

INDEX 935

Digitized by Google

LIST OF PLATES

PLATE		FACING PAGE
1.	Malaria Parasites (*colour*)	32
2.	The Blood Picture in Quartan and Mixed Infections (*colour*)	34
3.	Benign Tertian Malaria	36
4.	The Blood Picture in Benign Tertian Malaria (*colour*)	38
5.	The Blood Picture in Subtertian Malaria (*colour*)	40
6.	Subtertian Malaria: Sections of Brain and Liver (*colour*)	44
7.	Two Well-known Malaria-carrying Anopheles (*colour*)	92
8.	Blackwater-Fever Urine (*colour*)	104
9.	Conorhinus megistus (*colour*)	142
10.	Tse-tse Flies (*colour*)	144
11.	Parasites of Kala-azar and Oriental Sore (*colour*)	150
12.	Ticks (*colour*)	186
13.	Stegomyia fasciata (*colour*)	210
14.	Dengue Rash (*colour*)	226
15.	Pellagra (*colour*)	372
16.	Pellagra Rash on Feet	374
17.	Intestinal Lesions in Amœbic and Bacillary Dysentery (*colour*)	408
18.	Microscopical Section of the Large Intestine in Bacillary Dysentery	410
19.	Sprue Tongue (*colour*)	476

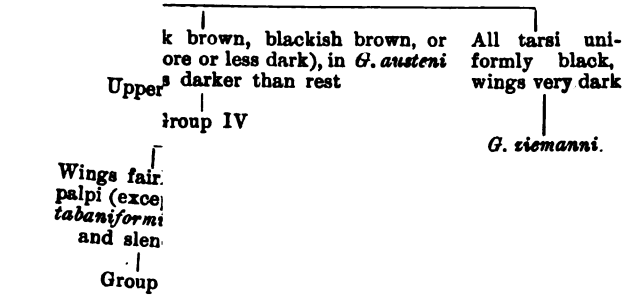
Digitized by Google

PLATE FACING

20. Early Macular Rash of Leprosy (*colour*) . .
21. Schistosoma Eggs . . . . . .
22. Schistosomiasis of the Far East . . . .
23. Microfilariæ of the Blood (*colour*) . . . .
24. Stegomyia pseudoscutellaris (*colour*) . . .
25. Distinguishing Features between mf. bancrofti and mf. loa, in Stained Specimens (*colour*) .
26. Tinea Imbricata . . . . . .
27. Normal and Abnormal Blood-cells (*colour*) . .

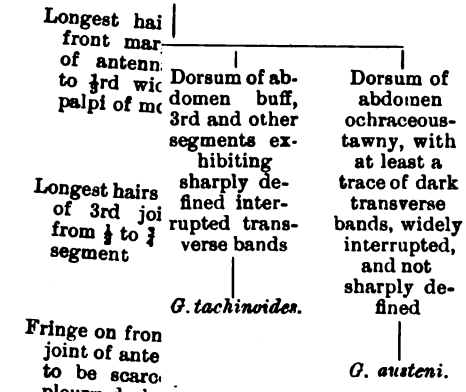
Digitized by Google

Digitized by Google



GLOSSINA IV

ALPALIS GROUP



NOTE.—*G. sever*
G. fus
definit as yet uncertain; although in some respects resembling recorded only from Cameroon, cannot be assigned to a

Digitized by Google

TROPICAL DISEASES

Section I.—FEVERS

CHAPTER I

MALARIA

Definition.—Morbid conditions produced by certain protozoal parasites belonging to the class Sporozoa, whose definitive host is the mosquito, and whose intermediate host is man. In man these parasites inhabit the red blood-corpuscles, giving rise to fever—usually of a periodic character, anæmia, enlargement of the spleen, and the deposit of a black pigment in the viscera and elsewhere. Some of their phases are amenable to quinine.

History

The history of malaria goes back to times of remotest antiquity. Already in the fifth century B.C. Hippocrates recognized the existence of periodic fevers, and divided them into quotidian, tertian, subtertian, and quartan.

The introduction of cinchona in 1640 enabled Morton and Tort to separate the malarial fevers from other febrile diseases, and to show that some continued and remitting fevers belong to the same group as the intermittents.

The next important step was the discovery of the characteristic pigmentation of the viscera in malaria. Certain pigment-bearing cells found in the spleen were described by Meckel in 1847, and their presence in the peripheral blood was later confirmed by Virchow and Planer.

The parasitic nature of malaria was definitely established by Laveran, who in 1880, having noticed the eruption of long motile filaments from the pigmented cells, first recognized their parasitic character.

Laveran's observations were soon extended by Marchiafava, Celli, Golgi, Bignami, Bastianelli, and other investigators.

Manson, impressed by the fact that a certain and very active

Digitized by Google

phase of the parasite was evolved, not while in the human body, but only when the blood containing the parasite had been removed from the human body, concluded that this phase represented the first step in its extracorporeal life; and he further reasoned from the analogy of other hæmoparasites and from ascertained epidemiological facts that certain species of mosquito were the agents that removed the parasite from the human body, and were the medium in which biological changes necessary for qualifying the parasite for re-entrance into a human host were effected. Ross's investigations on the lines suggested by Manson definitely established the accuracy of his hypothesis, and proved that the mosquito not only recovered from the human body the parasites, but also that it implanted them into the human host.

Finally, the application of these recent discoveries to the diagnosis and prevention of malaria has led to practical measures which have already been fruitful in good results and promise yet more.

Proofs that the Malaria Parasites are the Cause of Malarial Disease

It is now placed beyond doubt that the presence and proliferation in the blood of these parasites are the cause of what was formerly and is still known as "malarial disease." The reasons for this statement are now sufficiently well known. They are based upon the well-ascertained facts that the phenomena of malarial fever are invariably associated with parasites in the blood; that intravenous injection of parasite-containing blood into a normal individual is followed, after a period of 10–12 days, by an attack of fever and the appearance of the same species of parasite in the blood of the person thus injected; that the parasite undergoes developmental changes in the bodies of certain anopheline mosquitoes, and can be demonstrated at a later date in the salivary glands; that such a mosquito can convey the infection to a second individual after a definite incubation period; and further, that the drug quinine, which cures malarial disease, causes the parasites to disappear from the blood.

The proof of the causal relationship of the parasite to the disease may therefore be said to be complete.

Morphology and Histology

There are three species of malaria parasites. The distinctive characteristics of each of these will be detailed later. The following brief description is confined to what may be regarded as the generic features common to all.

Digitized by Google

The three phases.—The malaria parasite, like all true parasites, must be adapted not only for a life inside its hosts, but also, in order that its continuance as a species may be assured, for a passage from one host to another. Consequently, as regards man, it exhibits two distinct phases—an intracorporeal and an extracorporeal. Clinical observation and analogy make it certain that there is yet another phase, also intracorporeal—the latent phase, whose characters as yet can only be conjectured.

INTRACORPOREAL OR HUMAN CYCLE

Each species of malaria parasite has its special and more or less definite intracorporeal life-span or cycle of, approximately, forty-eight hours, or seventy-two hours.

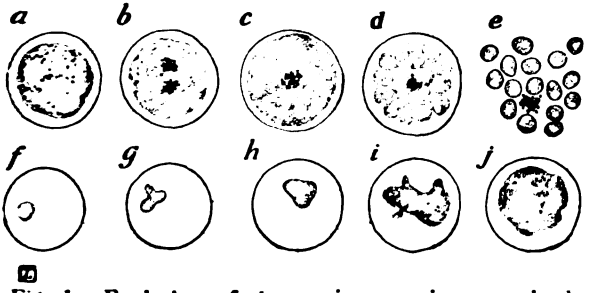


Fig. 1.—Evolution of the tertian parasite, unstained (*see* text).

On examining microscopically malarial blood towards the end of one of these cycles, an hour or two before the occurrence of a paroxysm of the characteristic periodic fever it induces, the parasite may be recognized as a pale, somewhat ill-defined disc of protoplasm occupying a larger or smaller area within a proportion of the red blood-corpuscles (Fig. 1, *a*). Scattered through this pale body are a number of intensely black or reddish-black particles—an excrementitious material called hæmozoin.

Changes in the parasite.—The changes the parasite undergoes may be followed by making repeated examinations of the blood at frequent intervals. As the parasite matures, the hæmozoin collects into central blocks round which the pale protoplasm of the parasite arranges itself in minute segments. The including corpuscle breaks down and liberates the spherules, or spores, none of which contains hæmozoin. A proportion of the spores, escaping phagocytosis, attach themselves to other red blood-corpuscles, which they contrive to enter. In the interior of these

Digitized by Google

newly infected corpuscles the young parasites grow at the expense of the hæmoglobin, and exhibit active amœboid movement. By appropriate staining the free spherules are found to consist of a nucleolus (a deeply tinted chromatic mass, surrounded by a vesicular nucleus), and this again by a lightly tinted covering of protoplasm. As the parasite grows and approaches maturity, the nucleolus enlarges, becomes less defined, and then disperses; finally, just before sporulation both nucleus and nucleolus cease to be distinguishable (Fig. 2, *a*, *j*).

At this stage these elements become fragmented and diffused throughout the protoplasm. Later the nuclear elements reappear as numerous minute, scattered nucleoli; and it is around these that the protoplasm of the segmenting parasite arranges itself to form the spherules (Fig. 2, *b*, *c*). The vesicular character of the

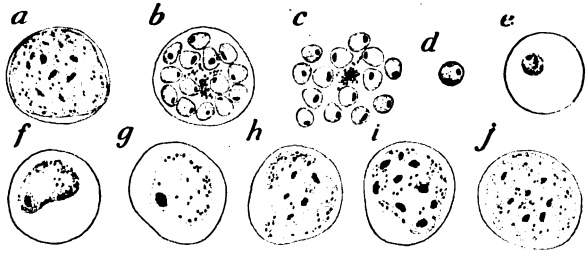


Fig. 2.—Evolution of the tertian parasite, stained (*see* text).

nucleus does not usually appear in the spherules until after these have become free in the liquor sanguinis (Fig. 2, *d*).

The hæmozoin particles, so characteristic of the malaria parasite, occur as black or very dark-red dust-like specks, coarse grains, or short rods, either isolated or aggregated into larger or smaller, more or less dense clumps. Until the concentration of hæmozoin which precedes the formation of spherules takes place the particles are scattered, being located principally in the outer zone, or ectosarc, of the parasite. Apparently, so long as the nucleus remains entire the hæmozoin is peripheral; when segmentation occurs in the nucleus the hæmozoin becomes central.

Such is a brief account of the cycle and structure of one phase of the parasite. From it we may understand how the parasite maintains itself and multiplies inside the human body. It does not explain, however, the two other important biological features which analogy and observation clearly indicate—namely, its latency in, and its life outside, the human body.

Digitized by Google

EXTRACORPOREAL OR MOSQUITO CYCLE

The problems suggested by the question of an extracorporeal cycle for the malaria parasite are—first, how does the parasite leave the human body; second, what is its life when temporarily outside the human body; and, third, how does the parasite re-enter the human body?

The flagellated body.—When fresh malarial blood is examined some time after it has been mounted as a wet preparation, it is no unusual thing to see what is known as the "flagellated body"* (Fig. 3). Analogous bodies are found *in all forms of*

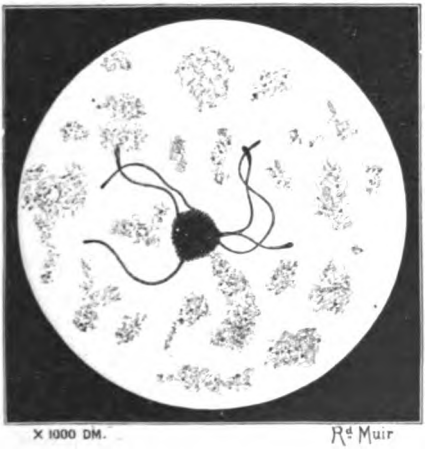


Fig. 3.—Malaria parasite: flagellated body, stained.

malaria, both in those special to man and in the corresponding infections of other vertebrata. It is a strange-looking, octopus-like creature with long, actively moving arms. Though composed of the same materials—namely, colourless protoplasm and dark hæmozoin granules—it differs in many respects from the ordinary forms of the parasite, more especially in the fact that it is not intracorpuscular, but free in the liquor sanguinis. The long, whip-like arms, numbering from one to six, or even more, are usually designated flagella or, more correctly, microgametes. These are

* The expressions "flagellated body" and "flagellum," applied to this phase of the malaria parasite, though graphic enough, are somewhat misleading. The flagella of the malaria parasite are in no sense analogous to the flagella of the flagellata; they really function as spermatozoa. The proper zoological terms for this and the other phases of the malaria parasites are given at p. 19.

Digitized by Google

exceedingly delicate and pliant filaments, difficult to see not only on account of their delicacy but also on account of the rapidity of their movements. Occasionally it may be observed that one or more of the microgametes break away and may be seen swimming away with vibratile and undulatory movements. (Fig. 4.)

It is of importance to bear in mind that these flagellated bodies are never seen in newly drawn blood, and that they come into view only after the slide has been mounted for some time—ten to thirty minutes, or even longer, according to circumstances.

Source of the flagellated body.—Careful observation shows that the flagellated bodies are developed from a particular phase

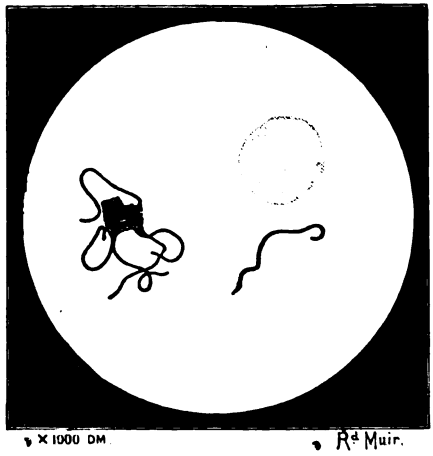


Fig. 4.—Malaria parasite; flagellated body and free-swimming microgamete.

of the intracorpuscular parasite, a phase which differs in form according to species—namely, in the subtertian type from what is known as the "crescent body"; in other types from certain analogous intracorpuscular parasites closely resembling the mature parasite (Fig. 2, *j*) just prior to concentration of hæmozoin and segmentation.

The crescent body.—These mature parasites are never found in the blood at the commencement of a malarial attack, but only after 7–10 days; they are not affected by quinine. They may be very numerous, several in every field of the microscope, or so scanty that many preparations may have to be searched before one is found. Not infrequently they cannot be discovered at all; especially is this the case in malignant (subtertian) infections in

Digitized by Google

the tropics, although, strange to say, when the same patients suffer a relapse in Europe it is generally easy enough to find the crescent body in the blood.

The shape, size, and structure of the crescent body can best be comprehended from the illustrations (Figs. 5, 6). It exhibits no amœboid movements. The principal features to be noted are its very definite crescentic shape; the probable existence of a delicate limiting membrane; the presence of needle-shaped hæmozoin particles, usually about the centre of the parasite, though sometimes nearer one end; and a bow-like and exceedingly delicate line that, springing from a point somewhat inside the rounded-off tips of the horns of the crescent, bridges its concavity. Manifestly this bow represents the outline of the remains of the blood-corpuscle in which the parasite had developed. Very rarely twin or double crescents—that is, two crescents in one corpuscle—are encountered (Fig. 5).

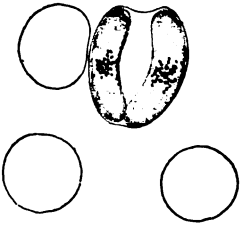


Fig. 5.—Malaria parasite: twin crescents.

Crescents differ in appearance according to their age; in some the hæmozoin granules are scattered throughout the parasite, in others they are concentrated, and in a third class the protoplasm shows vacuolation and other signs of degeneration. By dissolving the hæmozoin particles at the centre of the crescent with weak solution of ammonia, and subsequently staining, a nucleolus, sometimes double, can be demonstrated.

As will be shown in the sequel, these crescent bodies and the large intracorpuscular forms just alluded to are sexual in their functions. As regards the crescents, there are certain differences in the appearance of the protoplasm, in the arrangement of the pigment, and in the characters of the nucleus as revealed by staining, which are distinctive of the male and female crescents respectively. In one type of crescent the protoplasm is hyaline and the hæmozoin somewhat loosely arranged; in another type the protoplasm is faintly granular and the hæmozoin more concentrated, being arranged as a well-defined ring about the centre of the parasite. The former is male, the latter female. The protoplasm of the male parasite stains less deeply, and its nucleus is larger than that of the female parasite.

The more immature forms of the crescent are said to begin to be recognizable in the spleen and bone-marrow about the fourth day after a subtertian malarial attack commences. At first they

Digitized by Google

are minute, highly refringent amœboid bodies. They are rarely encountered in peripheral blood; there the crescent body does not begin to show itself till it approaches maturity, about a week after the first crop of amœboid parasites associated with the fever paroxysm has appeared.

Formation of the flagellated body from the crescent in subtertian, and from the large intracorpuscular parasites in quartan and tertian malaria.—If a number of crescent bodies are kept under observation a certain proportion will be seen to become gradually converted into spheres (Fig. 7, *a*, *b*, *c*). The

Fig. 6.—Female crescent in subtertian malaria. × 1,000.
(*Microphoto: Dr. A. Norman.*)

remains of the enclosed blood-corpuscles fall to pieces or melt away. The ensuing sphere is now known to be of two sexes, some—the male—having hyaline, others—the female—having granular protoplasm. After a time, in the case of the former, the hæmozoin particles become violently agitated and are diffused through the sphere, and one or more filaments are shot out from the periphery and indulge in wavy or lashing movements (Fig. 7, *e*).*

* Careful focusing, especially of stained crescent-derived spheres, may sometimes show that for a short time before their eruption the microgametes exist preformed inside the limiting membrane of the sphere (Fig. 7, *e*). One can sometimes see a microgamete filament, in its efforts to erupt, carry this membrane in front of it, and, failing to break through, retract and perhaps renew the effort at another point. Doubtless the agitated movements of the sphere are produced by the efforts made by the microgametes to break through this membrane.

Digitized by Google

The granular spheres, or the female element, do not project filaments, or microgametes. In stained specimens the microgametes are found to be composed of two elements—a chromatic filament enclosed in a covering of protoplasm. Should the microgametes succeed in breaking away, the remains of the flagellated body

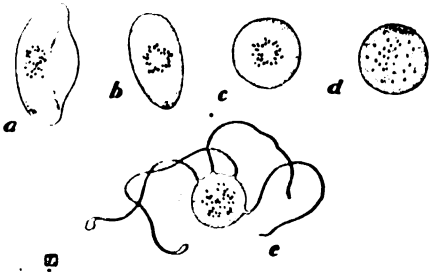


Fig. 7.—Evolution of the flagellated body from the crescent.

consist of hæmozoin particles included in a small amount of residual protoplasm.

In quartan and benign tertian malaria certain bodies (Fig. 8, *a*, *d*), which, but for the brisk movements of their hæmozoin, look like ordinary full-grown intracorpuscular parasites prior to

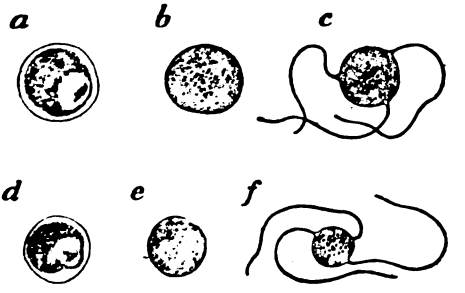


Fig. 8.—*a*, *b*, *c*, Evolution of the flagellated body in tertian fever; *d*, *e*, *f*, evolution of the flagellated body in quartan fever.

the formation of spores, may sometimes be seen to slip out from their enclosing corpuscles (Fig. 8, *b*, *e*). If these free parasites are watched, in some instances the hæmozoin they contain is seen to indulge in violent dancing movements, the body of the parasite being at the same time agitated and jerked about. Finally, "flagella" (microgametes) may be suddenly projected from the periphery (Fig. 8, *c*, *f*), very much in the same way as they are

Digitized by Google

projected from the periphery of the crescent-derived sphere. Manifestly, these large spherical parasites and the flagellated bodies arising from some of them correspond to the crescent-derived sphere and crescent-derived flagellated body.

Conditions favouring and retarding eruption of microgametes.—By exposing the slide to the air with slight aqueous admixture, as by breathing on the slip before applying the cover-glass, it is generally easy to procure quickly, from crescent-containing blood, specimens of the flagellated body.

In certain bloods the flagellated body is easily procured; in others the opposite is the case. As regards the crescents, doubtless success depends in a measure on the degree of maturity of the parasite, young or effete crescents failing to evolve. There are other conditions affecting the process, however, which are as yet unknown.

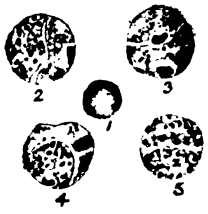


Fig. 9.—Abnormal malaria parasites.

(*After Dr. J. D. Thomson, "Jl. R.A.M.C."*)

1, Normal red corpuscle; 2, gametocyte and schizont; 3, gametocyte and gametocyte; 4, gametocyte and schizont; 5, schizont and schizont, both undergoing schizogony.

Double infection of red cells.—Occasionally, though rarely, sporulating and sexual forms of the malaria parasite may be seen inhabiting the same red corpuscle. The appearance thus produced is very puzzling, and gave rise to the theory put forward by Schaudinn that a process of "parthenogenesis" was apt to occur in the case of the malaria parasite, and that this would explain the "latent stage" of that organism. These bodies (Fig. 9) have been accurately described and figured by J. D. Thomson, and their nature is now perfectly clear. (*See also* Plate I., B, 8.)

Mosquito-Malaria Theory

Popular and early views.—The idea that some relationship exists between the mosquito and malaria has long been entertained, not only by medical men but also by the inhabitants of malarial countries. This was a popular belief in Italy, as well as in East Africa. King and others many years ago pointed out how a mosquito-malarial hypothesis could best explain the epidemiological facts of malaria, but as to how the mosquito intervened they had no reasonable explanation to offer. Laveran, Koch, and Pfeiffer also expressed similar views. It remained for Manson first to offer a definite hypothesis.

A mosquito-malaria theory definitely formulated.—In 1894,* and again in 1896, Manson formulated a definite hypothesis

* *Brit. Med. Journ.*, December 8th, 1894; "Goulstonian Lectures," *Brit. Med. Journ.*, March 14th, 21st, and 28th, 1896.

Digitized by Google

on the subject. Being a parasite, the germ of malaria, to keep in existence as a species, must pass from host to host; in other words, must at some time have an extracorporeal life. From the fact that the flagellated body does not come into existence until the blood has left the blood-vessels—that is, until it is outside the body—he concluded that the function, then unknown, of the flagellum lay outside the human body, and that the flagellated body was the first phase of the extracorporeal life of the malaria parasite. As the parasite, whilst in the circulation, is always enclosed in a blood-corpuscle, and is therefore incapable of leaving the body by its own efforts, and as it is never, so far as is known, extruded in the excreta, he concluded that it is removed from the circulation by some blood-sucking animal, most probably by some suctorial insect common in the haunts of malaria. This blood-sucker he believed to be the mosquito, an insect whose habits seemed adapted for such a purpose, and whose distribution conformed to the well-ascertained habits of malaria. Further, basing his argument on what he had shown to be the fact in the case of *Filaria bancrofti*, and on the peculiarities of the distribution of malaria, he reasoned that only particular species of mosquito were capable of subserving particular species of malaria parasite.

Ross's observations.—Ross, to whom Manson suggested the investigation of this hypothesis, first (1895) demonstrated the fact that when crescent-containing blood is ingested by the mosquito a large proportion of the crescents rapidly proceed to flagellation and to the emission of microgametes. In 1897 he showed that, in a particular species of mosquito fed on malarial blood, living and growing malaria parasites containing hæmozoin are to be found embedded in the stomach wall of the insects. Early in 1898 he showed that if a particular species of mosquito be fed on the blood of plasmodium-infected birds, the parasite, which both in habit and structure closely resembles the malaria parasite of man, enters the stomach wall of the insect, grows and sporulates there, that the resulting sporozoites subsequently enter the salivary gland of the insect, and that the insect is then capable of infecting by its bite other birds. Ross further showed that only particular species of mosquito could subserve the avian plasmodium in this way, and that the particular mosquito in question was not efficient as regards another blood parasite of birds—namely, hæmoproteus—or as regards the malaria parasites of man. Thus, by direct observation and by analogy, Ross distinctly, and first, proved that the extracorporeal phase of the malaria parasite is passed in particular species of mosquitoes, and, by

Digitized by Google

analogy, that the parasite is transferred from man to man by the mosquito.

MacCallum's discovery.—A gap in Ross's observations was filled in by MacCallum, who showed, principally by observations on hæmoproteus, also a malaria-like parasite of birds, that the function of the filament after it breaks away from the parent sphere, or flagellated body, is to impregnate the granular crescent-derived spheres, which are then transformed into sharp-pointed travelling vermicules (Fig. 15, 1). Doubtless, although the process has not been directly observed, it is in virtue of the locomoting and penetrating properties of the travelling vermicule that the malaria parasite is enabled to lodge itself, where Ross first found it, in the stomach wall of the mosquito.

Confirmation and extension of Ross's work.—Ross's observations were quickly confirmed and elaborated by the Italians, by Daniels, and by Koch. Grassi has shown that several species belonging to the genus *Anopheles*, more particularly—at all events as regards Italy—*Anopheles maculipennis*, are the special mosquito hosts of the malaria parasites of man. Step by step he traced the crescent-forming and the non-crescent-forming malaria parasites through their mosquito hosts, finding that in their evolution they closely resembled that which Ross had so successfully demonstrated for the avian plasmodium, and had so clearly foreshadowed and partly demonstrated for the malaria parasite of man. In conjunction with Bignami he repeated successfully in man Ross's experiment of conferring malarial disease by mosquito bite. Bastianelli, Celli, Dionisi, Buchanan, and many others have confirmed Ross's statements, and have added to our knowledge of the extracorporeal cycle of the malaria parasite.

Finally, on behalf of the Colonial Office and the London School of Tropical Medicine, with the assistance of Drs. Sambon and Low, Manson instituted two experiments which disposed for good and all of any objections that otherwise might have been advanced against the theory. Drs. Sambon and Low, Mr. Terzi, their servants and visitors, lived for the three most malarial months of 1900 in one of the most malarial localities of the Roman Campagna—Ostia—in a hut from which mosquitoes were excluded by a simple arrangement of wire gauze on the doors and windows. They moved freely about in the neighbourhood during the day, exposed themselves in all weathers, drank the water of the place, often did hard manual work, and, beyond retiring from sunset to sunrise to their mosquito-protected hut, observed no precautions whatever against malaria. They took no quinine. Although their neighbours, the Italian

Digitized by Google

peasants, were each and all of them attacked with malaria, the dwellers in the mosquito-proof hut enjoyed an absolute immunity from the disease. While this experiment was in progress, mosquitoes fed in Rome on patients suffering from tertian malaria were forwarded in suitable cages to the London School of Tropical Medicine, and on their arrival were set to bite the late Dr. P. Thurburn Manson and Mr. George Warren. Shortly afterwards both of these gentlemen, neither of whom had been abroad or otherwise exposed to malarial influences, developed characteristic malarial fever, and malarial parasites were found in abundance in their blood, both at that time

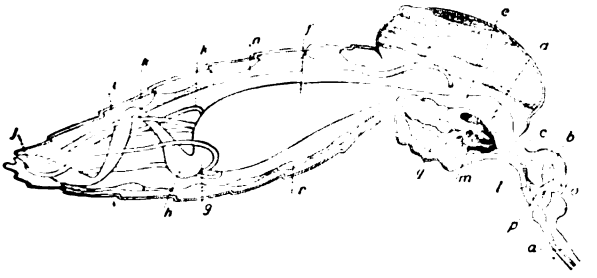


Fig. 10.—Section of mosquito.

a, Mouth; *b*, pumping organ; *c*, œsophagus; *d*, homologue of proventriculus; *e*, anterior part of midgut; *f*, midgut; *g*, pylorus; *h*, pyloric diverticulum; *i*, hindgut; *j*, rectum; *k*, Malpighian tubes; *l*, salivary duct; *m*, salivary gland; *n*, dorsal vessel; *o*, supraœsophageal ganglion; *p*, subœsophageal ganglion; *q*, conjoined ganglia; *r*, abdominal ganglia.

and on the occurrence of the several relapses of malarial fever from which they subsequently suffered.

The mosquito-malaria theory, therefore, passed from the region of conjecture into that of fact.

The Malaria Parasite in the Mosquito
(*See* Figs. 10–16)

In the lumen of the stomach: travelling vermicule stage. —When blood containing either subtertian crescents or mature endocorpuscular forms of the benign tertian or quartan parasite has been ingested by certain species of mosquito belonging to the Anophelinæ, those bodies that are mature are transformed into the two types of sphere already described—hyaline and granular; that is to say, male and female. The hyaline spheres then emit their filaments or microgametes, which, breaking away, approach and seek energetically by butting and boring to enter the granular spheres. At one point on the surface of each of the granular spheres a minute papilla is projected to meet, as it were, a corresponding attacking microgamete. At this point one of the latter

Digitized by Google

contrives to enter, and, after momentarily causing considerable perturbation in the contents of the sphere, comes to rest and vanishes from view. Although the granular sphere may be subsequently energetically attacked, no second microgamete can effect an entrance. For a short time after this act of impregnation the granular sphere or macrogamete undergoes no apparent

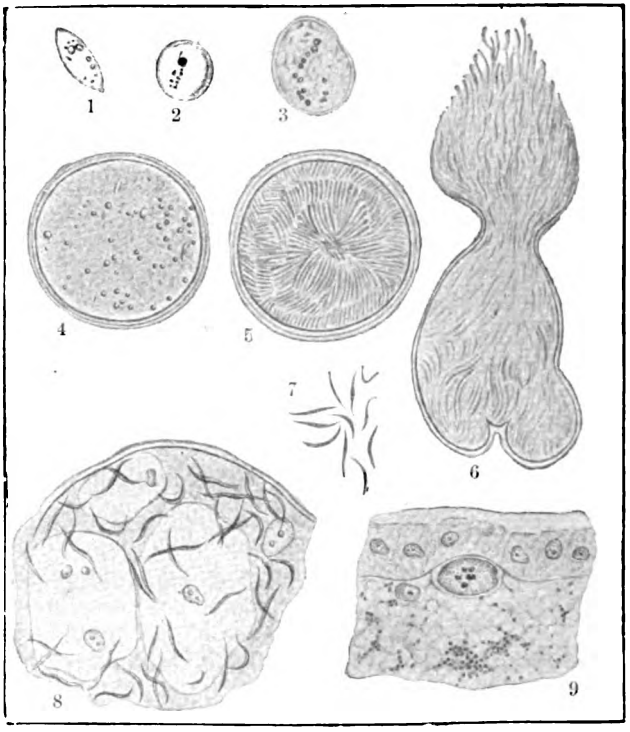


Fig. 11.—Evolution of the crescent parasite in Anopheles maculipennis.
(Adapted from Grassi, Bignami, and Bastianelli.)

1 to 6, The parasite as found in the stomach wall; 7, isolated sporozoites; 8, sporozoites in the salivary gland; 9, section of stomach wall showing the parasite *in situ*.

change. Presently, however, it gradually alters in shape, becoming oval, elongated, and finally assuming a lanceolate and then a vermicular form, the hæmozoin accumulating at the broad or posterior end whilst the anterior end becomes pointed and hyaline. On the completion of these changes the little body begins to move about, at first slowly, then more rapidly, the pointed end being in front. Should this travelling vermicule, technically known as an

Digitized by Google

oökinete, impinge on a blood-corpuscle, white or red, it passes through it.

Exact observations by Christophers have shown that, under the most favourable circumstances, at the maximum only about 4 per cent. of a suitable anopheline intermediary host (*Anopheles culicifacies*) are found naturally infected. Roubaud indicates that *A. maculipennis* is a most propitious intermediary for both *P. vivax* and *L. malariæ;* he found that 39·37 per cent. of the insects became infective with the former, and 50 per cent. with the latter parasites, when fed in captivity upon a suitable case. The insects are best kept in a wooden cage (p. 926) and fed upon glucose solution on cotton-wool. The experience of Wenyon in Salonica and that of the Editor in England would indicate that, given a suitable benign tertian case, fully 80 per cent. of the *A. maculipennis* develop oöcysts in their stomachs, often in very large numbers, if kept moist and at 70° F. For technique of dissection of these insects, *see* the Laboratory Appendix, p. 925.

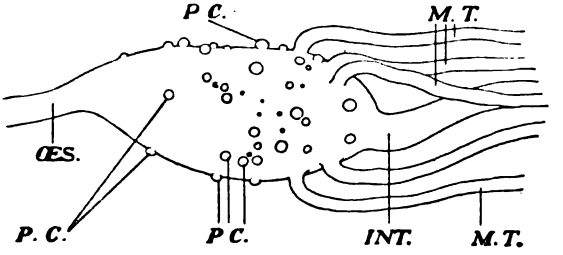


Fig. 12.—Stomach after infection with P. vivax.

M.T., Malpighian tubes; INT., intestine; ŒS., œsophagus; P.C., oöcysts protruding into the body cavity.

In the stomach wall: encysted or zygote stage (Fig. 11). —This newly acquired power of locomotion and penetration on the part of the fecundated parasite, together with other well-ascertained facts, justifies the presumption that soon after its formation the travelling vermicule, now known as an oökinete, penetrates the wall of the mosquito's stomach. Working its way through the layer of cells and the delicate basement membrane which together constitute the inner coat of this organ, it finally lodges itself among the longitudinal and transverse muscular fibres lying between this inner membrane and the equally delicate outer coat. Here the parasite, some thirty-six hours after the mosquito has fed, may be detected as a minute (6 μ) oval or spherical body with a sharp outline and hyaline or slightly granular contents in which the hæmozoin particles are plainly visible. It lies between the muscular fibres, which, as it grows, it disrupts to a certain extent.

During the next few days the parasite increases rapidly, acquiring

Digitized by Google

a well-defined capsule, and, in consequence of its growth, protruding on the surface of the insect's stomach like a wart or wen (Figs. 12, 13). Meanwhile, important changes take place in the interior of the parasite, which has now acquired a spherical contour and has attained the stage of development to which the term oöcyst is applied. Nucleus and protoplasm divide into a sort of a sponge-work with protoplasmic masses, around which, attached by one end like the spines on a porcupine, a vast number of minute

Fig. 13.—Transverse microscopic section of stomach of Anopheles maculipennis with numerous oöcysts in presporozoite stage.
(From a preparation by C. M. Wenyon.)

(16 μ), slender, spindle-shaped, nucleated bodies are ultimately formed. At a later stage the spherules disappear, leaving the spindles (sporozoites) loose in the capsule, which is now packed to bursting-point. In about a week—sooner or later according to atmospheric temperature, which has a great influence on the rate of development of the parasite—the capsule ruptures and collapses, discharging its contents into the body cavity of the mosquito.

The investigator, on dissecting anopheles, should have no difficulty in recognizing malarial oöcysts, even under a low power of the microscope. They are spherical and very refractile, appearing to jut out beyond the

Digitized by Google

stomach cells. With a higher power ($\frac{1}{8}$ lens) the characteristic pigment can be seen in their interior. In *P. vivax* it is light yellow, and in *L. malariæ* dark brown in colour. There are various misleading appearances which one must learn to recognize, such as certain large body cells, known as pancreatic cells, gregarine cysts, and even encysted larval trematodes, which occur in the stomach of these insects.

In the salivary gland: sporozoite or infective stage.—From the body cavity of the mosquito the spindle-shaped sporozoites pass, probably by way of the blood of the insect,

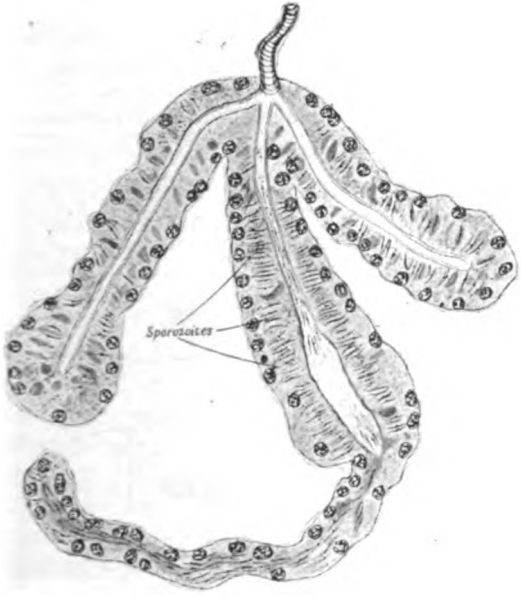


Fig. 14.—Salivary gland of Anopheles maculipennis containing sporozoites of Laverania malariæ, compiled from serial sections.
(From a preparation by C. M. Wenyon.)

to the three-lobed salivary glands lying one on each side of the fore part of the thorax of the insect (Figs. 10, *m*, 15, 3, and 16, *B*). These glands communicate with the base of the mosquito's proboscis by means of a long duct, around the radicles of which the clear, plump cells of the gland are arranged. The sporozoites can be readily recognized in many (Fig. 11, 8), though not in all, of the cells, especially in those of the middle lobe, and also free in the contents of the ducts. So numerous are they in some of the cells that the appearance they present is suggestive of a bacillus-laden lepra cell.

Digitized by Google

Transference to the Human Host

By a large number of experiments, abundantly confirmed, Ross distinctly proved that, if appropriate birds are bitten by mosquitoes

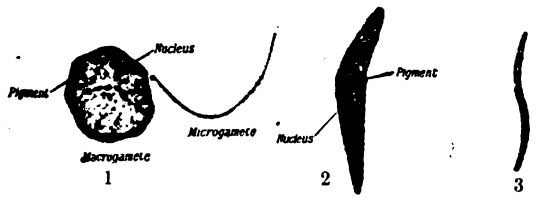


Fig. 15.—Evolution of Lavernia malariæ in Anopheles maculipennis. Highly magnified. (*After Wenyon.*)

1, Fertilization of macrogamete by microgamete of L. malariæ; 2, oökinete of L. malariæ from stomach of A. maculipennis twelve hours after feeding; 3, sporozite from salivary gland of A. maculipennis; wet preparation.

whose salivary glands contain the sporozoites of the avian plasmodium, the birds become infected with the parasite, and in due course show it in their blood and develop corresponding clinical

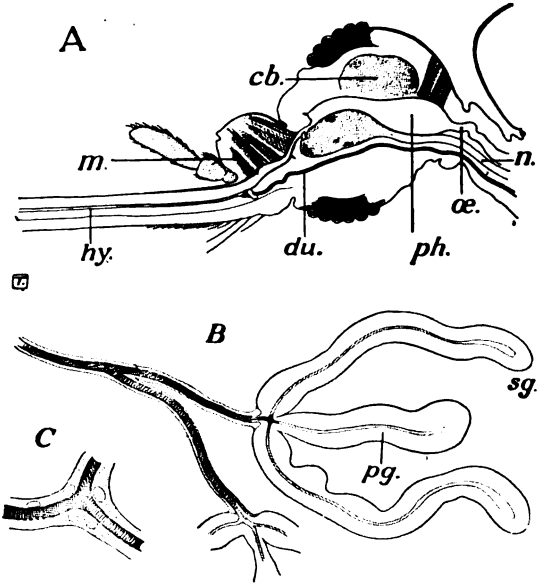


Fig. 16.—Dissection of head of mosquito.

A, Median section of head, showing *du*, the veneno-salivary duct, with its insertion in *hy*, the hypopharynx; *cb*, cerebrum; below this are the cerebellum and the pumping enlargement of *œ*, the œsophagus; *m*, muscle; *n*, nerve commissure. The other parts have been removed. *B*, the veneno-salivary duct, showing its bifurcation and the three glands on one of its branches; *pg*, poison gland; *sg* marks the upper of the two salivary glands. *C*, The bifurcation of the duct with its nucleated hypodermis.

Digitized by Google

symptoms. And now many experiments, some of which have been alluded to, have clearly shown that a similar process occurs in the evolution of the malaria parasite. If a mosquito whose salivary glands contain malarial sporozoites bites a man, the sporozoites are introduced into the blood, penetrate the red corpuscles, and multiply. After eight to ten days their progeny can be seen as malaria parasites of the type corresponding to those of the man on whom the infecting mosquito had originally fed. Schaudinn, by diluting blood with blister serum and introducing into the mixture the salivary glands of a malaria-infected mosquito, was enabled to witness the entrance of the sporozoites into the red corpuscles.

Complete Cycles of the Parasites

The complete cycles (Fig. 17), therefore, both intra- and extra-corporeal, of the endocorpuscular blood parasites of man and birds can now be described. Using the most generally adopted zoological terms, and commencing with the youngest phase, these parasites may be described as entering the blood-corpuscles as *sporozoites*. Growing at the expense of the hæmoglobin they become pigmented and, on reaching maturity, develop either into (*a*) *schizonts* (the segmenting body—rosette body), or into (*b*) *gametocytes* (crescents, spherical bodies of benign tertians or quartans).

(*a*) The *schizonts*, after concentration of hæmozoin, divide into a number of naked segments, or *merozoites*, which, on the breaking down of the enveloping blood-corpuscle, escape into the blood plasma and enter fresh blood-corpuscles; thus completing the *endogenous cycle* and providing for the multiplication of the parasite in the vertebrate host. The process of reproduction in this the *asexual cycle* is called *schizogony*.

(*b*) The *gametocytes*, or *gametes* as they are usually termed, belong to the *exogenous* or *sexual cycle* passed in the bodies of particular species of mosquito. They are of two kinds, *male* (hyaline crescents or spheres) and *female* (granular crescents or spheres). The male gametocyte emits several *microgametes* (flagella), one of which, breaking away, enters and impregnates the single *macrogamete* of which the female gametocyte consists. The product is a *zygote*, which, acquiring locomoting powers, becomes an *oökinete*, and transfers itself from the lumen to the wall of the middle intestine (stomach) of the mosquito in which it had developed. Here it comes to rest and is soon surrounded with a capsule. It is now an *oöcyst*. Presently it divides into a number of daughter cells and *residual bodies*. The former produce a vast number—as many

Digitized by Google

as ten thousand in a single oöcyst—of minute bodies, the *sporozoites* (zygotoblasts, germinal rods—Ross). Finally the oöcyst ruptures, discharging the sporozoites into the body cavity of the insect, whence they are transferred to the salivary glands, in the secretion of which, opportunity offering, they are injected into the blood

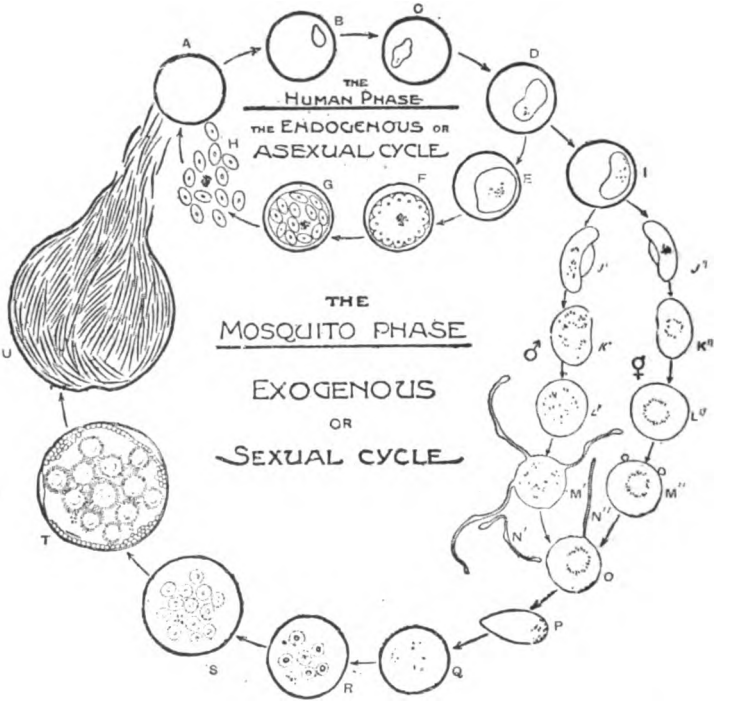


Fig. 17.—Schema showing the human and mosquito cycles of the malaria parasite. Modified from Blanchard's diagram illustrating the life-cycle of Coccidium schubergi. ("*Practitioner*," *March*, 1901.)

A, Normal red cell; B, C, D, E, red cells containing young parasites; F, G, H, schizogony; I, young gametocyte; J′, K′, L′, M′, microgametocytes or male gametes; J″, K″, L″, M″, O, macrogametocytes or female gametes; N′, N″, microgametes; P, travelling vermicule; Q, young zygote; R, S, oöcysts; T, oöcyst with plasmodial masses; U, mature oöcyst.

of an appropriate vertebrate, whose blood-corpuscles they subsequently enter, and, becoming schizonts, renew the cycle. The process of multiplication in this the sexual or exogenous cycle is called *sporogony*.

There has been a good deal of speculation as to why certain parasites develop into schizonts, whilst others become gametocytes. The circumstance of the late appearance of the gamete is looked

Digitized by Google

upon by some as evidence that the blood, from repeated development in it of swarms of endogenous parasites, has become exhausted as a pabulum, and that, in consequence of this, the parasite is directed to a line of development providing for life and growth elsewhere—that is the mosquito.

Latent phase.—It is a well-established fact that, concurrently with the subsidence of acute clinical symptoms, the malaria parasite may disappear from the general circulation. This it does either spontaneously or as a result of the administration of quinine. In the majority of instances the disappearance is only temporary. Usually, after an interval of weeks or months, the parasite reappears in the general circulation and there is a renewal of the clinical phenomena. As to the organ or tissue it selects, or as to its appearance and structure during this time of latency, or as to the exact conditions which cause it once more to resume active, propagating, circulating life, nothing is positively known.

Three opinions, each of them founded on a certain amount of fact, have been advanced on this point: (*a*) That the parasites, when the conditions become unfavourable for schizogony, become encysted and lie up in the spleen or other organ. (*b*) That they never completely leave the circulation, but continue to propagate in the usual way, though in numbers so small that it is practically impossible to find them even by prolonged microscopical examination. (*c*) That certain sexual individuals (macrogametes), a phase of the parasite apt to persist for prolonged periods in the blood, form parthenogenetically, and while still in the circulating blood, asexual spores (merozoites), which, on liberation, enter the red blood-corpuscles and so renew the asexual, intracorporeal phase. This much we do know—namely, that physiological strain or vital depression in the host tends to bring about conditions which break up, and that quinine and vital vigour tend to bring about conditions which favour, latency.

Possibility of yet Another Phase

So far the story of the life-history of these parasites seems to be complete. There are certain facts, however, which seem to indicate the possibility of yet another phase, or of etiological factors which hitherto have escaped observation. First, there are districts in India, Africa, and elsewhere that are practically uninhabited on account of the prevalence and virulence of the local malaria. If man be necessary for the completion of the life-cycle of the parasite, how explain its abundance in such circumstances—that is to say, in the absence of man? Second, those engaged in

Digitized by Google

malarious districts on works entailing disturbance of the soil—e.g. opening jungle lands, digging canals or foundations, making roads or railways—are particularly prone to contract malaria; yet such operations at first sight seem in no way calculated to foster broods of malaria-infected mosquitoes. How account for infection in such circumstances? where, and in what form, is the malaria germ to be found there?

Most observers are now of opinion that the malaria parasite, under natural conditions, can be acquired by man only through the bite of the mosquito; that the mosquito can acquire the parasite only by ingesting the blood of a malaria-infected man or, possibly, other mammal; that there is no extracorporeal life other than that described; that there is no authentic instance of malaria being acquired in uninhabited places; that, in the case of malaria in connection with soil disturbances, it depends on the creation during digging operations of puddles of water in which mosquitoes breed; and that its epidemic occurrence in these circumstances is owing to unhygienic conditions, such as usually prevail when large bodies of men, some of whom may bring the infection with them, are brought together on public works attended with extensive earth-cutting, as in railway, road, or canal making.

Microscopical Study of the Blood

Before commencing the study of malarial blood it is advisable for the beginner to familiarize himself with the microscopical appearances of normal blood, both in fresh and stained preparations. He should learn to recognize the several varieties of leucocyte; to appreciate differences in colour, size, and shape of the red cells; to recognize dirt, vacuoles, forms of crenation, and artificially-produced appearances. By mastering such details at the outset important sources of fallacy will be avoided, and in the process of self-education a useful knowledge of technique will be acquired.

For a thorough appreciation of the principles on which blood examinations for the demonstration and study of the malaria parasite should be conducted, it must be borne in mind that the parasite is intracorpuscular. To see it, therefore, it is necessary, particularly for the beginner, so to dispose the corpuscles in the preparations that a proportion of them shall lie flat on the slide in a single layer, and presenting their surfaces and not their edges to the observer. It is mainly from ignoring this fundamental principle that so many fail to find the parasite.

Technique.—The beginner will save time if he gets someone who is familiar with the necessary technique, and with the appear-

Digitized by Google

ance of the parasite in the blood, to give him one or two lessons. Accuracy and quickness can be acquired only by practice. It is a good plan to practise preparing films from one's own blood—for the details of which the reader is referred to Appendix III., p. 878.

The examination is best conducted with a $\frac{1}{12}$-in. oil-immersion lens, a rather low eyepiece, a sub-stage condenser, and a good but not too dazzling illumination. It is practically useless to work with any objective lower than $\frac{1}{12}$ in., or without a sub-stage condenser.

When the beginner has learnt to recognize the larger forms of the parasite, he will have begun to appreciate what sort of body he has to look for; thereafter he should be able to educate himself, and to pick out the smaller and intermediate forms.

In proceeding to make his first examination of a liquid-blood slide, the beginner, in the first instance, should confine his attention to the "single-layer zone." Field after field of this he must pass in review, carefully scrutinizing the interior of every blood-corpuscle, every leucocyte, and every pigmented body, even though it be not included in a corpuscle. He must not expect to find parasites in every corpuscle, or even in every field; and he certainly must not expect, as the beginner usually does, to find in every slide the beautifully regular segmenting form or "rosette body," or the weird-looking flagellated body made familiar to us by so many illustrations. Such bodies, though really present somewhere and in some form at one time or another in every case, are among the least common of the many phases of the malaria parasite; they are met with only under very definite and not very constantly encountered conditions, and are not very often seen at an ordinary clinical examination.

In most cases the parasite is discovered in the first field or two examined; but in not a few instances dozens of fields may have to be scrutinized before a single parasite is found. Therefore no examination can be said to be complete, in a negative sense, until at least half an hour has been spent over several suitably-prepared slides.

Phagocytosis and pigmented leucocytes. — Pigmented leucocytes—that is to say, leucocytes containing grains or blocks of hæmozoin—are often encountered; they can best be seen in the single-layer zone of the film during, or shortly after, fever. Leucocytes may sometimes be observed to include the hæmozoin set free by the falling to pieces of the segmented parasites. Often they derive their hæmozoin from the remains of some sphere or flagellated body which they may have engulfed

Digitized by Google

subsequently to the preparation of the slide. In peripheral blood the phagocytes are rarely, if ever, seen to attack the parasite so long as it is inside a blood-corpuscle.

Both the large mono- and, very rarely, the poly-nucleated leucocytes may contain malarial pigment. Care, however, must be exercised in drawing conclusions from the discovery of black material in these bodies; in imperfectly cleaned slides, fragments of dirt, which the leucocytes rapidly take up, are apt to mislead.

Diagnosis of vacuoles.—The beginner may have a difficulty in determining whether certain appearances in the corpuscles are vacuoles, or whether they are parasites. The following hints may help him to a correct decision: Vacuoles (Fig. 18, *a*, *b*, *c*, *d*, *e*, *f*, *h*,

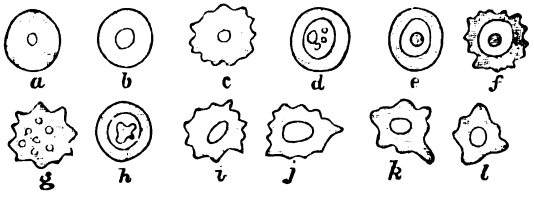


Fig. 18.—Vacuolated and crenated blood-corpuscles.
(After Laveran and Blanchard.)

a, *b*, *c*, Blood corpuscles with central vacuoles, *c* is crenated: *d*, *e*, *f*, *h*, blood corpuscles with central vacuole containing fragmented hæmoglobin. Sometimes minute eye-shaped vacuoles with a speck of hæmoglobin in the centre are met with, and are apt to be taken for parasites. *g*, Crenated blood-corpuscles with several vacuoles, or, it may be, crenations out of focus; *i*, *j*, *k*, *l*, deformed blood-corpuscles with central lacunæ.

i, *j*, *k*, *l*) are well defined, clear, and have sharp edges; they may change form slightly, but they have no true amœboid movement, carry no pigment, and, of course, do not stain. Intracorpuscular malaria parasites, on the contrary, are dim and, as a rule, ill defined; they have soft, shaded-off edges; possess amœboid movements; when large they carry hæmozoin grains; and, of course, they take the appropriate stains. It is hardly necessary to indicate the points of diagnosis from leucocytes, or from cupped, folded, or crenated (Fig. 18, *c*, *f*, *g*, *i*, *j*, *k*, *l*) corpuscles.

The parasite as a means of diagnosis.—All of these multiform appearances the student must learn to recognize and interpret. Skill in this is merely a matter of time, practice, and reflection. Given these, the student should be able not only to diagnose by the microscope malarial infection, but also to recognize the type of any particular infection, the period of the fever cycle, and, it may be, the severity of the case. For diagnosis in malaria, therefore, skill in the microscopical examination of the blood

Digitized by Google

is of the utmost value, and no pains should be spared by the practitioner in malarious countries to acquire it.

Bearing of quinine on microscopical diagnosis.— It is of little use to examine the blood for the intracorporeal forms of the malaria parasite after full doses of quinine have been taken; the drug rapidly brings about the disappearance of this phase of the parasite. The crescent alone is unaffected by drugs, and in suitable cases may be found for days after the patient is cinchonized.

On staining malarial blood. — As a general rule, the beginner should work only with unstained preparations of fresh liquid blood. To the unpractised, staining is full of pitfalls. In such circumstances it must not be relied on for purposes of responsible diagnosis. To the experienced microscopist and diagnostician, and for the study of the morphology of the parasite, staining is of the highest value; moreover, some such method must be employed should permanent preparations be desired, or should it be inconvenient to make an immediate examination of the blood. Many methods have been devised, and are described in Appendix III., pp. 881–4.

The many methods of obtaining differential staining of protoplasm and nucleus depend on the circumstance that, when solutions of certain kinds of methylene-blue and eosin are mixed, a third red dye, with a special affinity for chromatin, is formed. They are all modifications of the original Romanowsky method. They are a little uncertain and troublesome to use, their success depending on the purity of the chemicals employed and careful attention to detail. The beginner is advised to become proficient, in the first instance, with the simpler methods given in the Appendix.

On examining successful slides prepared by any of the Romanowsky methods, the red blood-cells will be found to be stained pale pink or greenish; the polynuclear leucocytes will show nuclear network ruby-red, the margins of the nuclei being sharply defined, whilst the protoplasm is unstained, except such fine eosinophile granules as it may contain, which are red; the mononuclears and lymphocytes have sharply defined ruby-red nuclei and faint blue protoplasm; the coarse-grained eosinophiles have a less deeply-stained ruby-red nucleus and pale pink granules; the basophiles have dark purple-black granules and ruby-red nucleus; nucleated red cells have almost a black and sharply defined nucleus; the blood-plates are deep ruby-red with spiky margins and sometimes a pale blue peripheral zone. The body of the malarial parasite is stained blue and the chromatin of the nuclei ruby-red; and in

Digitized by Google

deeply stained preparations of the tertian parasite the hæmoglobin of the including red blood-corpuscles will be dotted over with certain fine or coarse red granules known as Schüffner's dots.

Cultivation of the Malaria Parasite

The cultivation *in vitro* of the malaria parasite was first effected by Bass, in 1911, and subsequently confirmed by the brothers Thomson. The method is, briefly, as follows: 10 c.c. of aseptically drawn blood from the median basilic vein of an untreated malaria patient are immediately transferred to a large test-tube containing $\frac{1}{10}$ c.c. of a 50-per-cent. solution of Merck's dextrose. The tube is fitted with a cap through which runs a glass rod, and with this the blood is gently defibrinated. The mixture is distributed into culture tubes so as to form columns of about 2 in., and then incubated at 40° C. After a time it settles into three layers—an upper ($\frac{1}{2}$ in.) of serum, an intermediate ($\frac{1}{15}$ to $\frac{1}{20}$ in.) of red and white corpuscles, and a bottom of red corpuscles. It is only in the red corpuscles of the very thin intermediate layer that the parasites grow and multiply. They are absent from the serous or top, and they die in the bottom layer. The tubes should be examined at the end of twelve hours' incubation, after which time the parasites die out. By drawing off with a fine pipette a little of the middle layer the progress of the culture can be watched and subcultures started. To succeed with the latter, however, the leucocytes have to be removed by centrifugation. Strict asepsis and the avoidance of air-bubbles in drawing off and defibrinating the blood are indispensable. Chambelland has recently suggested the following modifications: Centrifuge the defibrinated blood, pipette off the serous and leucocytic layer, replace with physiological saline, and add 0·15 c.c. of a 50-per-cent. solution of glucose for 5 c.c. of original blood abstracted. Subcultures are made by adding one volume of the original culture, taken 1 mm. below the surface of the deposit, to five volumes of freshly-washed red blood-cells. The sexual cycle has not been cultivated.

Digitized by Google

CHAPTER II

DESCRIPTION OF THE VARIOUS SPECIES OF MALARIA PARASITE AND THEIR ASSOCIATED FEVERS

THE different clinical types of malarial disease are associated with different and corresponding species of malaria parasites.

Classification of parasites.—The different species have been classified according to—

1. The duration of their respective life-cycles inside the human body.
2. Their morphological characters.
3. The clinical phenomena they give rise to.
4. The results of inoculation experiments.

It may be said that, so far as these tests go, there is evidence of plurality of species. That is to say, a particular clinical type of malarial disease is associated with a parasite of definite morphological form and intracorporeal life-cycle, characters which are maintained when the parasite has been inoculated experimentally.

The forms of the malaria parasite, and of the diseases they give rise to, may be divided into two comprehensive groups—the *benign* and the *malignant*. A principal morphological distinction between these two is that, whereas the benign parasites never form crescent bodies, the malignant or subtertian parasite forms crescents; that is to say, the gamete of the benign parasites is a sphere or disc, that of the malignant parasite a crescent. A principal clinical difference between the two is that, whereas the benign parasites rarely give rise to pernicious attacks, the malignant parasite frequently does.

The benign parasites are of two kinds: one, the *quartan parasite*, having a cycle of seventy-two hours, causing a fever recurring every three days—*quartan fever*; the other, the *tertian parasite*, with a cycle of forty-eight hours, causing a fever recurring every two days—*tertian fever*.

The malignant parasite, though once supposed to contain several varieties, has one form, a pigmented parasite, the *subtertian*, or *æstivo-autumnal*, of approximately forty-eight hours' cycle.

Digitized by Google

We may arrange these parasites thus :—

Benign . . { Quartan / Tertian } Do not form crescents.

Malignant . Subtertian : Forms crescents.

A tabular statement of the characters of the three parasites appears on pp. 30, 31.

Clinical classification of malaria. — Formerly, malarial diseases were divided into quotidian, tertian, and quartan intermittents or agues, and remittents. But since it has been found that what was designated remittent fever is produced by either quartan, tertian, or subtertian parasites—the fact of intermittency or remittency being more or less a matter of accident—it has been considered advisable to expunge the term remittent fever as indicative of a distinct species of malarial disease. Any one of the three kinds of parasites enumerated may cause what was known as remittent fever. The intermittency or the remittency of any given fever depends, in great measure, on the simultaneousness or the reverse of the maturation of the swarm of parasites giving rise to it. If all the parasites present are of nearly the same age, they mature approximately simultaneously, and we have an intermittent; if they are of different ages, they mature at different times scattered over the twenty-four hours, and we have what was known as a remittent. Further, two generations of tertian parasites maturing on successive days will produce a quotidian fever, Tertiana duplex; two generations of quartan parasites maturing on successive days will produce fever fits on two successive days followed by one day of freedom, Quartana duplex; three generations of quartan parasites will produce what clinically appears to be a quotidian fever, but in reality is a Quartana triplex.

Clinical Phenomena of Malarial Fever

Before proceeding with a description of the various malaria parasites and their associated fevers, there are certain generalities which, to save repetition, had better be mentioned here.

Intermittent fever or ague.—Every typical malarial fever is made up of a series of pyrexial attacks which recur at definite intervals of twenty-four, forty-eight, or seventy-two hours. Each attack consists of a stage of rigor, a stage of heat, and a stage of sweating; these are followed by a period, "the interval," of apyrexia—actual or relative. The duration and intensity of the constituent stages vary considerably. On the whole, they observe a certain proportion to each other; as a rule, the more pronounced

Digitized by Google

the rigor, the higher the fever and the more profuse the sweating. Such attacks, with well-marked intervals of apyrexia, are designated intermittent fevers or agues. The expression "ague" is applied only to intermittents having a pronounced rigor stage.

Premonitory stage.—Before rigor sets in, and sometimes for several days before the actual disease declares itself, there may or there may not be a premonitory stage marked by lassitude, a desire to stretch the limbs and to yawn, aching of the bones, headache, anorexia, perhaps vomiting, perhaps a feeling as of cold water trickling down the back. If the thermometer be used, it will be found that body temperature has begun to rise, it may be some two or three hours before the other and more striking symptoms which ensue set in; or it may be that the threatened attack will subside spontaneously without culminating in the more pronounced phenomena of a fully-developed ague.

Cold stage.—When rigor sets in, the feeling of cold spreads all over the body, becoming so intense that the teeth chatter and the patient shivers and shakes from head to foot. He seeks to cover himself with all the wraps he can lay hands on. Vomiting may become distressing. The features are pinched, the fingers are shrivelled, the skin is blue and cold-looking and may exhibit the condition known as "goose-skin" (cutis anserina). But the feeling of cold is entirely subjective; if the temperature be taken, it is found to be already several degrees above normal and to be rapidly mounting. In young children it is not at all unusual to have a convulsive seizure at this stage—a fact that has to be borne in mind, as it is very apt to lead to ideas of epilepsy.

Hot stage.—After a time the shivering gradually abates, giving place to, or alternating with, waves of warmth and, before long, to persisting feelings of intense heat and febrile distress. The wraps, which before were so eagerly hugged, are now tossed off; the face becomes flushed; the pulse is rapid, full, and bounding; headache may be intense; vomiting frequent; respiration hurried; the skin dry and burning, the thermometer mounting to 104°, 105°, 106° F., or even higher.

Sweating stage.—After one or more hours of acute distress the patient breaks out into a profuse perspiration, the sweat literally running off him and saturating his clothes and bedding. With the appearance of diaphoresis the fever rapidly declines; headache, vomiting, thirst, and febrile distress giving place to a feeling of relief and tranquillity. By the time the sweating has ceased the patient may feel quite well; a little languid, perhaps, but able to go about his usual occupation. The bodily temperature is now

Digitized by Google

often subnormal, and may remain so until the approach of the next fit, one, two, or three days later.

Duration of the fit.—The duration of an ague fit and of its constituent stages is very variable. On an average it may be put at six to ten hours, the cold stage occupying about an hour, the hot stage from three to four hours, the sweating stage from two to four hours.

TABULAR STATEMENT OF THE CHARACTERS OF

	Duration of development	Movement	Hæmozoin	Maximum size	Form of segmentation
1. Quartan parasite, *Plasmodium malariæ*	Seventy-two hours	Slight movement in the immature forms	Coarse grains; shows little or no movement	The size of the containing red blood-corpuscle	Daisy form; the single spores round, with distinct nucleolus
2. Tertian parasite, *Plasmodium vivax*	Forty-eight hours; or less in anticipating types	Active amœboid movement in the immature and also in the middle-aged forms	Finer granules in immature forms; often in the larger ones becoming very active	Size of a red blood-corpuscle; sometimes even larger	Sunflower or grape-like; single spores small, round; nucleolus rarely seen
3. Subtertian parasite, *Laveraniamalariæ* (*Plasmodium falciparum*)	Forty-eight hours or less	Active movement in the pigmented stage	Fine; often shows oscillatory movement	½–¾ the size of a red blood-corpuscle	Irregular heaps

The urine in ague.—During the cold stage the urine is often limpid and abundant, and is passed frequently; but during the hot sweating stages it is scanty, loaded, sometimes albuminous. The amount of urea is increased, particularly during the cold stage; and so are the chlorides and sulphates. The phosphates, on the contrary, diminished during the rigor and hot stages, are increased during defervescence. The augmentation in the excretion of urea commences several hours before the subjective symptoms of the attack begin, attains its maximum towards the end of rigor,

Digitized by Google

and decreases during the hot and sweating stages, although still continuing above the normal standard. The excretion of carbonic acid follows a corresponding course. Ringer was the first to point out the interesting fact that, although the return of fever may be prevented by the administration of quinine, yet, for a time, a periodic increase in the excretion of urea occurs on the days on which the fever fit was due. The urine is often deeply coloured,

THE THREE SPECIES OF MALARIA PARASITES

Number of mero-zoites	Form of gameto-cyte	Alterations in the infected blood-corpuscles	Relative number of parasites seen in peripheral and visceral blood respectively	Influence of quinine	Liability to reappearance of parasite after leaving infective regions
6-12	A sphere	The red blood-corpuscles are little discoloured, and are not materially altered in size; some appear smaller	Parasites seen in peripheral circulation throughout the whole cycle, and in as great numbers as in visceral blood	Causes disappearance of parasite readily	Liability persists for a very long period.
15-24	A sphere	The red blood-corpuscles are often hypertrophied, and lose colour. Schuffner's dots in deeply stained specimens	Parasites seen in peripheral blood throughout the whole cycle, but not in such large numbers as in visceral blood	Causes disappearance of parasite readily	Liability persists for long period.
10-12, generally more up to 32	A crescent	The red blood-corpuscles shrink frequently; they are dark, or may be almost colourless	An enormously greater number of parasites present in internal organs as compared with peripheral blood. The latter part of the cycle takes place in internal organs only	Causes disappearance of parasite less readily	After a few months, relatively less liability to recurrence.

giving with nitric acid the play of colour characteristic of bile pigment, or the brown colour described by Grübler as "hæmapheic," and contains the pigment urobilin, which may be detected both by chemical and spectroscopic tests (Appendix III., pp. 908–10). It may be taken as an index of latent malaria. Glycosuria does occur, but is by no means common.

The spleen during the fit.—The spleen becomes enlarged to a greater or less extent during rigor. At first the swelling disappears in the interval, but it tends to become more or less of a chronic

Digitized by Google

feature if the attacks recur frequently, more especially if they are associated with pronounced cachexia.

Period of the day at which ague commences.—Two-thirds of agues come off between midnight and midday. This is a fact to remember in diagnosis; especially when we have to face the possibility of recurrent pyrexial attacks being dependent on such conditions as liver abscess, tuberculosis, and septic states—conditions, be it remarked, in which febrile recurrence takes place almost invariably during the afternoon or evening.

Atypical agues.—Cases are frequently met with in which all the above symptoms are very much toned down; in which, perhaps, a periodically recurring feeling of coldness, followed by languor, or a slight headache, or a slight rise of temperature, is the only symptom indicating the presence of the malaria parasite in the blood. In some fevers, and these by no means the least dangerous, the subjective symptoms may at first be of so mild a character that the patient is able to go about his duties with a body temperature of 103° or 104° F.; he may have no severe rigor, no headache, no severe gastric symptoms, no acute febrile distress of a disabling character. Some of the African fevers—so liable to assume suddenly a pernicious character—are of this nature. On the other hand, notwithstanding a comparatively slight rise of temperature, headache, prostration, or vomiting may be extremely distressing. There is an infinite variety in this respect. Evidently the toxin—if toxin there be—of the malaria parasites is far from being a simple body; probably, like tuberculin, it contains several ingredients arranged in different proportions in the several species and varieties of the parasite. Doubtless, also, the degree of infection, various combinations of the species of parasite, and individual idiosyncrasy play a part in determining the intensity and character of the reaction of the human body to the toxin.

Terms employed.—Acute malarial attacks which recur daily are called *quotidian ague;* if they recur every second day, they are called *tertian ague;* if every third day, they are called *quartan ague.* As a rule, the attacks tend to occur about the same time every day. In some cases the time of recurrence becomes earlier each day; such fevers are said to *anticipate.* Or they may occur at a later hour; in which case they are said to *postpone.* When the individual paroxysms are prolonged, so that one attack has not concluded before the next commences, the fever fits are said to be *subintrant.* When the fit is prolonged and periodicity is marked by only a slight fall of temperature, a slight sweating, a slight feeling

Digitized by Google

PLATE I.

MALARIA PARASITES. × 2,000 diam.

(*Leishman's stain.*)

A.—SUBTERTIAN PARASITE (*Laverania malariæ*).

Fig. 1.—Subtertian rings, heavy infection. Note the marginal form, and in some the double chromatin dots.
Fig. 2.—Parasites twelve hours old, approximately, from a brain smear. At this stage they become arrested in the capillaries. Note early and characteristic concentration of pigment.
Fig. 3.—Parasite twenty-four hours old, from an artificial culture; forms seen usually in the capillaries of internal organs.
Fig. 4.—Complete schizogony, with separation of merozoites, from spleen smear.
Fig. 5.—Complete schizogony, from brain smear of a fatal case.
Fig. 6.—Male gametocyte (crescent), with remains of red cell, from peripheral blood.
Fig. 7.—Female gametocyte (crescent), staining a darker hue, with concentration of chromatin and pigment.
Fig. 8.—Exflagellation of male gametocyte.

B.—BENIGN TERTIAN PARASITE (*Plasmodium vivax*).

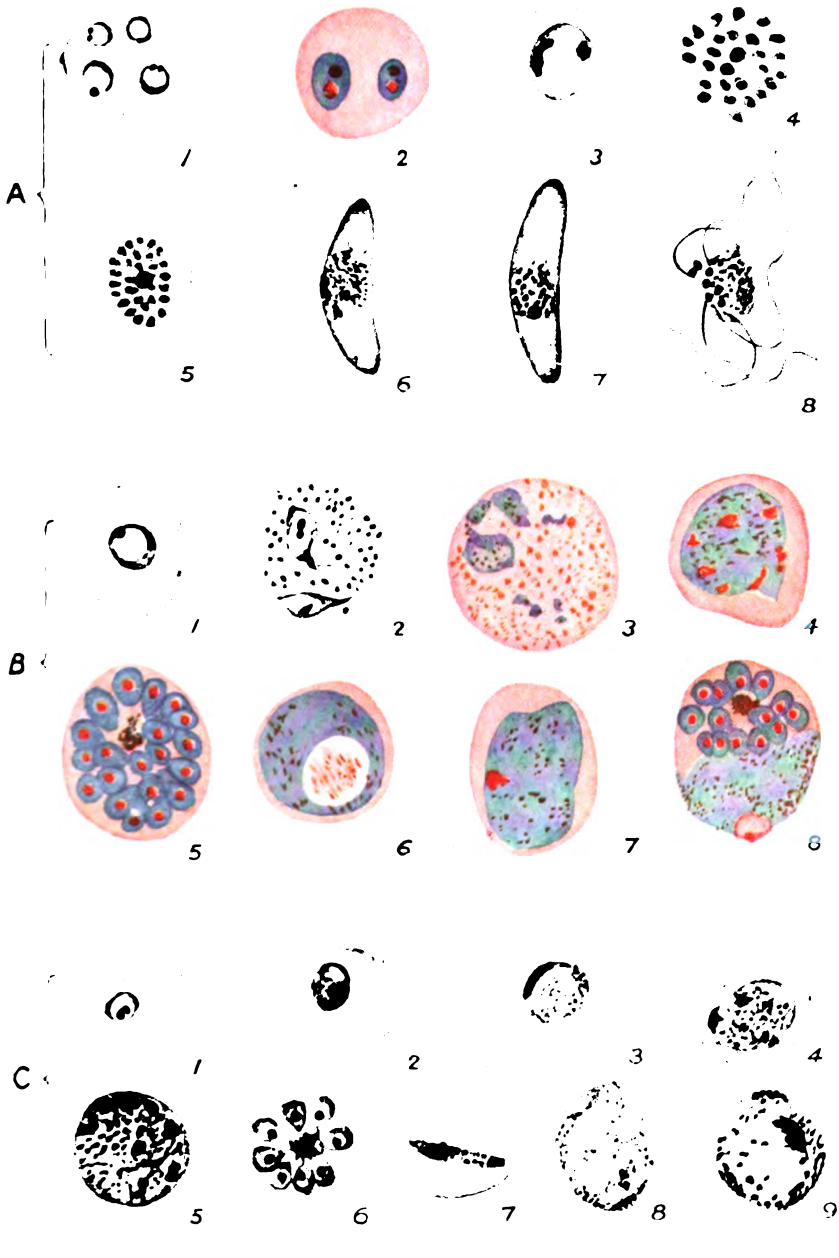
Fig. 1.—Young ring form in peripheral blood.
Fig. 2.—Amœboid forms. Note the Schüffner's dots and a slight enlargement of corpuscle.
Fig. 3.—Amœboid form, a quarter grown. Note formation of pigment in cytoplasm, Schüffner's dots, and increased size of corpuscle.
Fig. 4.—Schizont, showing early division of chromatin.
Fig. 5.—Complete schizogony in peripheral blood, with formation of twenty merozoites.
Fig. 6.—Male gametocyte. Note loose arrangement of chromatin, pale cytoplasm, and smaller size than female.
Fig. 7.—Female gametocyte. Note compactness of chromatin, and darker-staining cytoplasm.
Fig. 8.—Double infection of single corpuscle with gametocyte and schizont.

C.—QUARTAN PARASITE (*Plasmodium malariæ*).

Fig. 1.—Young ring form.
Fig. 2.—Partially-grown form; compact parasite with coarse pigment.
Fig. 3.—A more fully-grown stage than Fig. 2.
Fig. 4.—Early division of chromatin in young schizont.
Fig. 5.—More fully-grown schizont, with chromatin divided into eight masses. Note coarse and scattered pigment.
Fig. 6.—Complete schizogony, showing typical rosette with centrally-placed pigment and formation of eight merozoites.
Fig. 7.—Characteristic "band form" of young quartan parasite.
Fig. 8.—Male gametocyte.
Fig. 9.—Female gametocyte, with coarser pigment and darker-staining cytoplasm.

Digitized by Google

Digitized by Google



John Gerdon Thomson, pinx.

MALARIA PARASITES

PLATE I.

Digitized by Google

Digitized by Google

of chilliness, the fever is said to *remit*—to be a *remittent*. Sometimes there is no remission; such a fever is said to be *continued*.

All sorts of blendings of subtertian and tertian, and occasionally with quartan as well, may occur; such an infection is said to be *mixed*.

Relation of the phenomena of the fever fit to the stages of the parasite.—All the differences and peculiarities in the clinical phenomena of a malarial attack, complicated and hard to interpret in many cases though they be, are, it is believed, directly correlated to the phases of the intracorporeal life of the parasite; this organism is, in fact, the key to their interpretation. As already mentioned, as the time of rigor approaches, the pigment of the parasite, hitherto scattered throughout the substance of the little animal, becomes concentrated, and segmentation proceeds. Shortly before and during rigor, and as a direct cause of rigor, these segmented parasites are breaking up and, presumably, liberating their toxins. At the end of rigor, during the hot and during the sweating stages, the young parasites of the new generation—the small intracorpuscular bodies, and the leucocytes carrying the hæmozoin liberated at the breaking up of the segmented bodies—are in evidence, and the toxins liberated at the same time are being eliminated. During the interval the intracorpuscular parasites grow, become pigmented, and prepare for maturation. From the fact that parasites are present in the blood during apyrexia, and often in great abundance, it is evident that it is not the mere presence of the parasite in the blood-corpuscle that causes the fever; most likely, as suggested, the pyrogenic agent is some toxin which is liberated and becomes free in the liquor sanguinis on the breaking up of the parasite. Consequently, we find that in remittent and continued types of malarial fevers segmenting parasites may be met with at all stages of the fever; and, conversely, that when parasites at all stages of development are met with, the associated fever is probably remittent, irregular, or more or less continued in type.

The foregoing are generalities which apply to all the types of malarial infection.

Quartan Infection (Plates I., II.)

The parasite.—The parasite of quartan fever, *Plasmodium malariæ* (Fig. 19), has a cycle of seventy-two hours. At its earliest stages of epicorpuscular and of early unpigmented intracorpuscular life it takes the form of a small, roundish, clear speck (Plate I., C, 1), showing up somewhat distinctly against the hæmoglobin

Digitized by Google

of the invaded corpuscle. At this stage, as contrasted with the other species of malaria parasites, it is further distinguished by the feebleness of its amœboid movement. Later, as soon as it becomes pigmented (Fig. 19, *b*, *c*, *d*, *e*, *f*), all amœboid movement ceases (*see also* Plate I., C, 2, 3, 4, 7), and it grows across the corpuscle in its transverse diameter, giving it a characteristic ribbon-shaped appearance. Relatively to the other malaria parasites, the hæmozoin carried by the quartan is large in amount and coarse in grain, sometimes forming short rods. The segmented or mature parasite (Fig. 19, *g*, *h*) is made up of eight to ten elements arranged daisy-fashion and, generally, very symmetrically around the now centrally placed and massive block of very black hæmozoin. About the centre in each of the spherical or pear-shaped segments, which

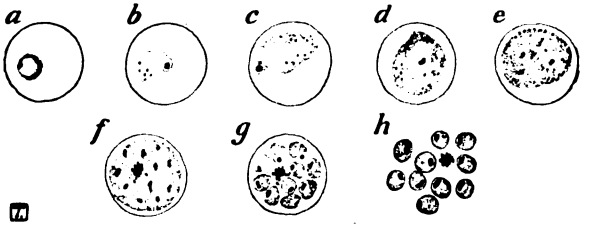


Fig. 19.—Quartan parasite, asexual stage : stained.

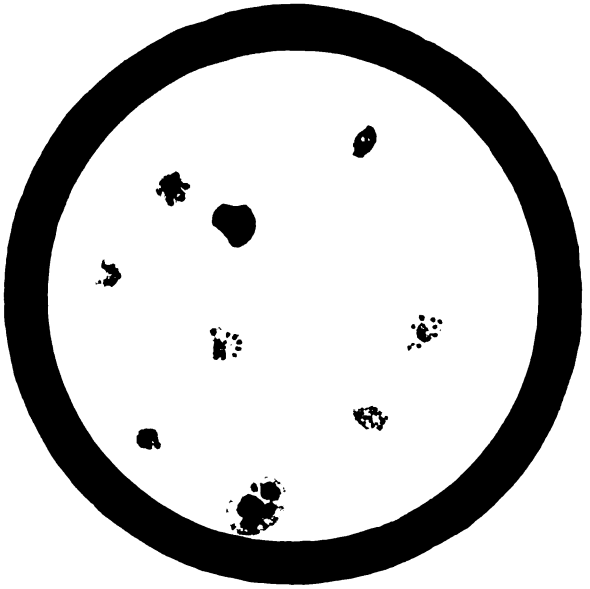
are slightly rough in outline, a shining nucleolus can usually be readily made out.

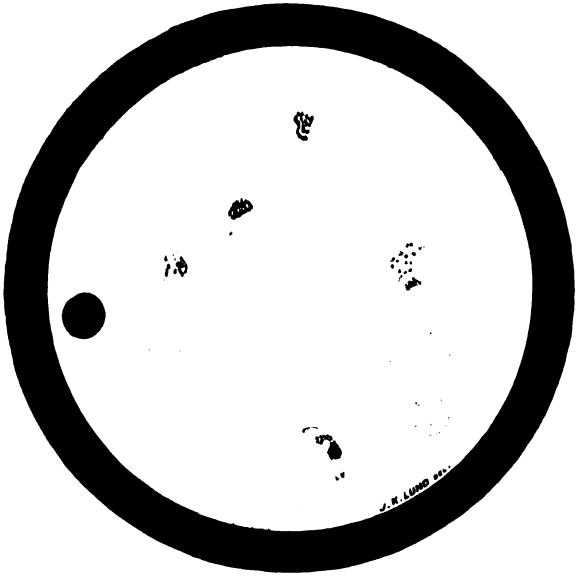
The gametocyte, or sexual form, is a spherical pigmented body looking like an ordinary large intracorpuscular pigmented parasite (Fig. 8, *c*) that has escaped from the red corpuscle in which it had developed. It may be recognized sometimes by the very active movement of the hæmozoin granules. This phase, rarely seen, occurs almost exclusively during the pyrexial stage of the cycle. Further, the quartan parasite does not, as does that next to be described—the tertian parasite—cause marked enlargement of the blood-corpuscle in which it lies ; on the contrary, the including corpuscle has often a shrunken appearance, with hæmoglobin darker than normal. When mature it completely fills the normal-sized corpuscle, scarcely a rim of hæmoglobin being visible (Fig. 19, *f*), so that it sometimes looks at this stage as if it were a free and independent body floating about in the liquor sanguinis.*

The "daisy"—as it is sometimes called—or segmented phase

* In malarial blood the corpuscles are apt to vary in size, as in other anæmic conditions. A quartan parasite in a megalocyte may therefore simulate a tertian. Usually the including blood-corpuscle is, or seems, smaller than normal.

Digitized by Google





(*J. K. Lund, del.*)

Fig. 1.—Blood-film of quartan parasite, showing sporulating bodies and developmental forms.

Fig. 2.—Blood-film of a double infection with the benign and subtertian parasite, showing crescents and developing benign forms.

THE BLOOD PICTURE IN MALARIA. QUARTAN AND MIXED INFECTIONS.

(*Gaudicheau's stain.*)

PLATE II.

Digitized by Google

Digitized by Google

of the quartan parasite is more frequently seen in the peripheral blood than is the corresponding phase of the other malarial parasites. For this reason, and because of the easy visibility of the parasite at all its stages owing to its size and to the large amount of hæmozoin it carries, and because the entire intracorporeal cycle is completed in the peripheral blood, the quartan is the best form of malaria parasite for the beginner to study.

Geographical distribution.—The fever which the quartan parasite gives rise to—single, double, or treble quartan ague—

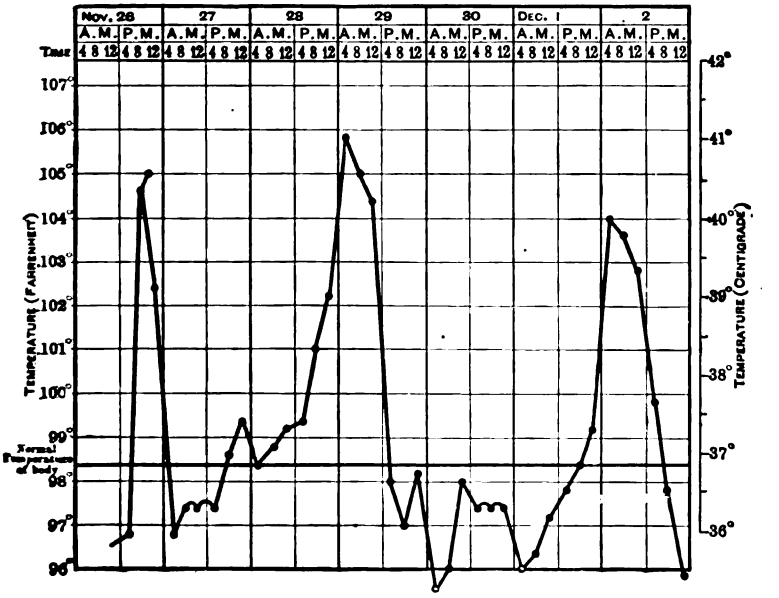


Chart 1.—Quartan ague.

is, relatively, much more common in temperate latitudes than in the tropics. Formerly it was common enough in England; it is still far from rare in the malarious districts of north and mid-Europe and, doubtless, elsewhere under similar climatic and telluric conditions. But as we proceed south it becomes, relatively to the other forms of malaria, rarer. In the tropics in some highly malarious places it is unknown. It is common enough in Southern India and the Andaman Islands, and is the dominating species in certain malarious districts of Ceylon and the Malay States. It occurs in Mauritius, Palestine, East Africa, and Sierra Leone. Though relatively rare in many of the West India Islands, it is a

Digitized by Google

common form in Antigua. The general statements that quartan ague is, relatively to the other forms of malaria, more a disease of the temperate zones than of the tropics, and, further, that both in the tropical and temperate zones it has topographically a very limited distribution, probably express the truth.

The fever.—The ague fit in quartan is generally smart while it lasts, and well defined as regards its constituent stages (Chart 1). It does not tend so markedly, as is the case with the other malarial infections, to the rapid development of cachexia. Although the individual attacks are very amenable to quinine, the infection appears to be of a more persistent nature than that of tertian and subtertian malaria; attacks, therefore, are prone to recur during several years.

Tertian Infection (Plates I., III., IV.)

The parasite.—The early stage of the benign tertian parasite, *Plasmodium vivax* (Plate I., B), resembles that of the quartan, inasmuch as it consists of a small pale speck on, or in, the invaded red blood-corpuscle (Plate I., B, 1); it differs in exhibiting very much greater amœboid activity, changing its form and location in the corpuscle incessantly, besides pushing out and retracting pseudopodia (Plate I., B, 2). This amœboid activity persists during growth and the formation of hæmozoin, though in a progressively diminishing degree; it gives rise to great and rapidly changing irregularities in the contour of the parasite (Plate III. and Fig. 1, *g*, *h*, *i*), but is almost entirely suspended by the time hæmozoin-concentration is effected. In the tertian parasite the hæmozoin particles are, on the whole, finer than those of the quartan parasite; and, moreover, are in a state of much more active and incessant movement, constantly changing their position in the peripheral region in which they, for the most part, seem to lie (Plate I., B, 6). Another, and highly characteristic, accompaniment of tertian infection is the considerable hypertrophy and marked decoloration of the corpuscles containing the parasite (Plate I., B, 2, 3, 5). Sometimes the affected corpuscles seem nearly twice the diameter of the healthy ones; and nearly always, if the parasite is of any magnitude, the rim of hæmoglobin has a "washed-out" look, sometimes being almost colourless.

In corpuscles invaded by the tertian parasite, deep coloration with Leishman's or Giemsa's stain brings out a feature which does not occur in those attacked by quartan or subtertian parasites. With these stains in tertian-invaded corpuscles the hæmoglobin is speckled with chromophilic particles called "Schüffner's dots."

Digitized by Google

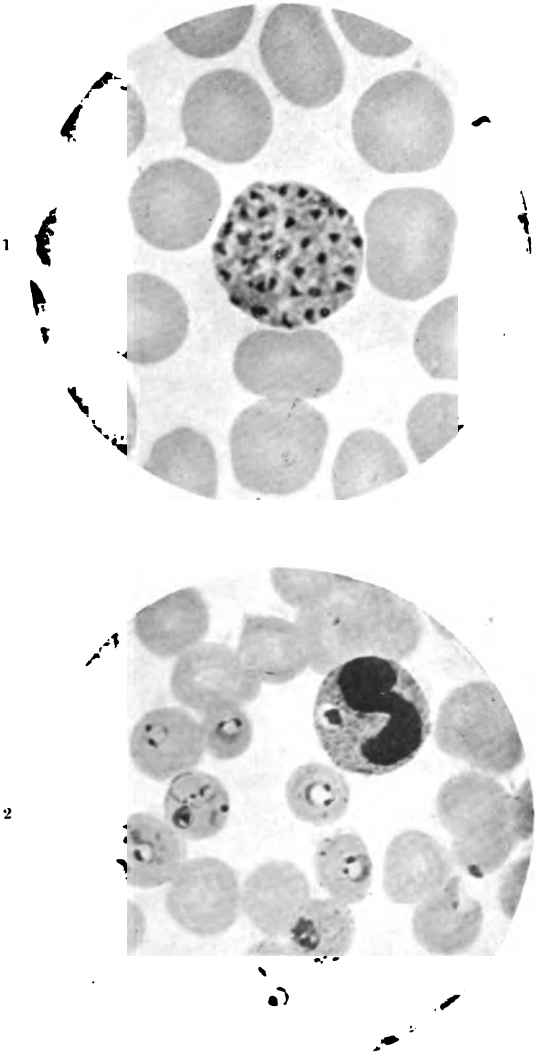


Fig. 1.—Sporulating body. × 1,500. (*Microphoto: Dr. J. Bell.*)

Fig. 2.—Benign tertian rings, Schüffner's dots, and a pigmented leucocyte. × 1,000. (*Microphoto: Dr. A. Norman.*)

BENIGN TERTIAN MALARIA.

PLATE III.

Digitized by Google

Digitized by Google

This is a feature of some diagnostic value. In the very young phases of the parasite it is not always present; unfortunately for its diagnostic value, these are just the phases that are difficult to diagnose from quartans and subtertians. (Plate III.)

In the tertian parasite, when segmentation is completed, the resulting body, instead of the very symmetrical, daisy-like figure of the quartan, resembles rather a cluster of grapes in some more or less central part of which one or two masses of dark pigment

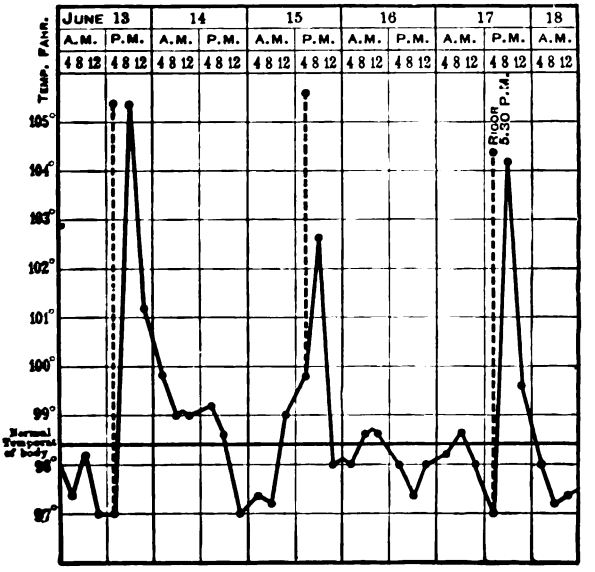


Chart 2.—Benign tertian ague.

have accumulated among the berries (Plate I., B, 5; also Figs. 1, *d*, 2, *b*). The little spherules forming the cluster—fifteen to twenty-six in number—are smaller, smoother, and more spherical than those of the quartan parasite; seldom, in the unstained condition, exhibiting their nuclei. It has been suggested that in natural, uncompressed conditions the tertian "rosette," as it is called, tends to pass from the disc form, impressed on it originally by the shape of the corpuscle, to something more approaching a globular form.

In the tertian, as in the quartan parasite, the gametocyte is a spherical body resembling closely the mature parasite from which the segmented body is evolved (Plate I., B, 6, 7). It is seen more particularly, just as in the case of the quartan infection, after and

Digitized by Google

not infrequently about the time of rigor. The tertian gametocyte is considerably larger than that of the quartan and subtertian parasite.

Geographical distribution.—The tertian parasite, probably the commonest form of malaria parasite, occurs in temperate and tropical latitudes alike. It is often met with as a double infection, and is, perhaps, the most frequent cause of quotidian as well as of tertian agues.

The fever.—The fever it gives rise to, except in the matter of the spacing—which is one of forty-eight hours—resembles that caused by the quartan parasite (Chart 2).

Subtertian or Malignant Infection (Plates I., V.)

The parasite (*Laverania malariæ—Plasmodium falciparum*, Blanchard).—One notable feature in the differentiation of the subtertian from the benign parasites is its much smaller size. The earlier unpigmented phase, owing partly to minuteness, partly to its forming but a thin and very transparent object in the hæmoglobin, is difficult to see (Fig. 20, *a*). When first mounted on the slide the amœboid movements are very active. The chromatic nucleolus is often divided into two—a very characteristic feature in stained preparations—distinguishing it from the younger forms of the benign. Multiple invasion of individual corpuscles is often encountered, and this much more frequently than in the benign infections, doubtless owing to the prodigious number of parasites present in malignant infections. As development advances, the invaded corpuscles seem to be filtered out by the capillaries and small arteries of the deeper viscera and of the bone-marrow. So that even in severe infections the later pigmented stages are by no means proportionately represented by, or even frequently encountered in, finger-blood; the segmenting form still less so (Fig. 20, *f*). To find numerous examples of the more advanced stages of these parasites it is necessary to aspirate splenic blood; or to search in fatal cases in the deeper viscera, or in the bone-marrow, liver, and spleen, immediately after death (Fig. 20, *c*, *d*, *e*). Owing to this absence of the more advanced forms from the peripheral circulation, the duration of the life-span of these parasites is difficult to fix; probably it is about thirty-six hours, but this is not very constant.

The sporulating or segmenting stage is very rarely encountered in the peripheral blood. It is composed of a variable number of *merozoites*, varying from eight to thirty-two, more usually the latter (Fig. 20, *g*, and Plate I., A, 5). The associated hæmozoin

Digitized by Google

(*J. K. Lund, del.*)

Fig. 1.—Blood-film showing parasite in various stages. × 1,000 diam.

Fig. 2. — Blood-film showing sporulating bodies and gametocytes. × 1,000 diam.

THE BLOOD PICTURE IN BENIGN TERTIAN MALARIA. (*Leishman's stain.*)

PLATE IV.

Digitized by Google

Digitized by Google

is dark in colour and disposed in an irregular heap. The infected blood-corpuscle may be altered in colour and may be either darker or lighter; sometimes it shrinks, or may become what is termed a "brassy body."

The crescent-shaped gametocyte is a characteristic feature (Plate I., A, 6, 7). These bodies are not seen at the commencement of an infection. Once they begin to appear they generally tend to increase in number during a few days. They may persist for one to six weeks after the associated fever, whether spontaneously or in consequence of the administration of quinine, has subsided. Quinine may prevent the appearance of crescents, yet when they are once formed the drug has little influence on these bodies or on their capacity for emitting microgametes.

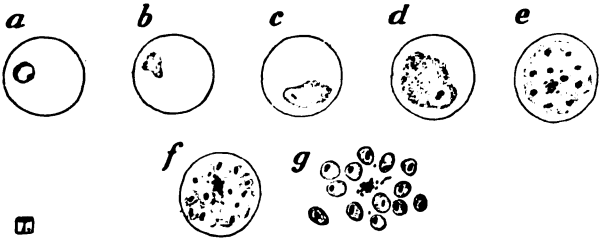


Fig. 20.—Evolution of the subtertian parasite: asexual cycle.

It is a singular fact that in many of the worst types of tropical malaria—as that of tropical Africa—crescents are few in number, and in some instances cannot be found by ordinary examination. Plehn states that during a period of two years in Africa he only once saw the flagellated body. On the other hand, when we meet with these African infections in England crescents are frequently encountered, and often in great abundance; at all events, this is a general experience. In primary infections under suitable conditions, crescents appear in the peripheral blood about the third week.

Characters of the fever.—It is found that the fevers produced by the malignant parasites are apt to be very irregular in their course. *The rigor stage is relatively less marked;* the pyrexial stage is more prolonged, and is often characterized by a tendency to adynamic conditions, together with vomiting, intestinal catarrh, pains in the limbs, anorexia, severe headache, and depression. After apparent recovery from the fever there is a great proneness to relapse at more or less definite intervals of from eight to fourteen days, but an immunity soon appears to develop. Experience

Digitized by Google

during the Great War has tended to show that benign tertian infections are far more persistent than are the subtertian. Subtertian fevers are accompanied by rapid destruction of corpuscles, and are usually followed by marked cachexia. At any time in their course, but more especially after primary infections, symptoms of the gravest character may declare themselves.

As a general rule the associated symptoms are, in many respects, very different from those caused by the tertian parasite. In the first place, although rigor is not so marked, the hot stage lasts longer —often exceeding twenty-four hours; in fact, the tendency for

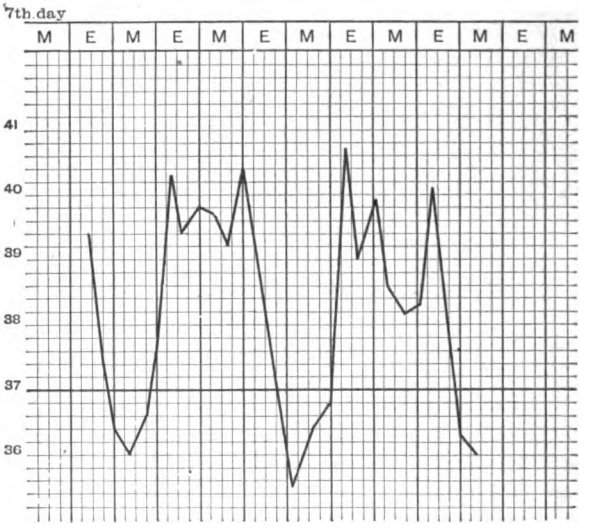
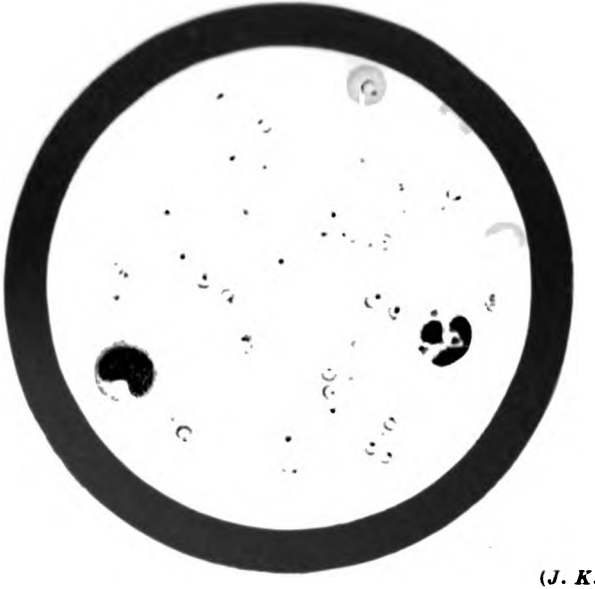
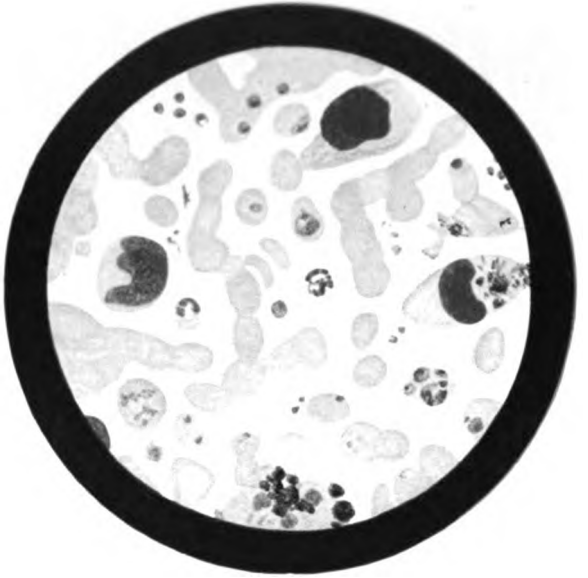


Chart 3.—Subtertian fever (L. malariæ).

the successive paroxysms to overlap, to become subintrant, is very marked. Moreover, when the intermissions are distinct, as Marchiafava and Bignami point out, the crisis is generally unlike that of ordinary tertian. There is frequently what is called a *double crisis;* that is to say, when the fever has attained its apparent fastigium there is a drop of one or more degrees of temperature—the "false crisis"—to be followed by a fresh rise, which is then succeeded by the "true crisis." This peculiar phenomenon the writers referred to attribute to the presence of two swarms of parasites, one of which matures somewhat later than the other, and is only proved to occur in one other tropical fever, namely, kala-azar. (Chart 3.)

Digitized by Google





(*J. K. Lund, del.*)

Fig. 1.—Blood-film from fatal case of subtertian malaria, showing heavy "ring" infection. (*Giemsa's stain.*)

Fig 2.—Spleen smear from same case, showing large numbers of developing parasites, sporulating bodies, and malarial pigment. (*Leishman's stain.*)

THE BLOOD PICTURE IN SUBTERTIAN MALARIA. × 1,000 diam

PLATE V.

Digitized by Google

Digitized by Google

A double infection of the subtertian parasite may produce a quotidian fever (Chart 4), a typhoid-like depression generally being a marked feature.

Geographical distribution.—Subtertian malaria is confined to the warmer regions of the earth, and to the more intensely malarial districts in these; hence the name "tropical" which has been applied to this type of infection. In the subtropical zones it occurs as a first infection only in late summer or early autumn; hence the name "*æstivo-autumnal.*" This peculiarity, as regards seasonal and geographical distribution, of subtertian malaria may be explained by the fact that for its development in the mosquito the subtertian parasite demands a higher atmospheric temperature than suffices for the quartan and tertian parasites. Hence, although

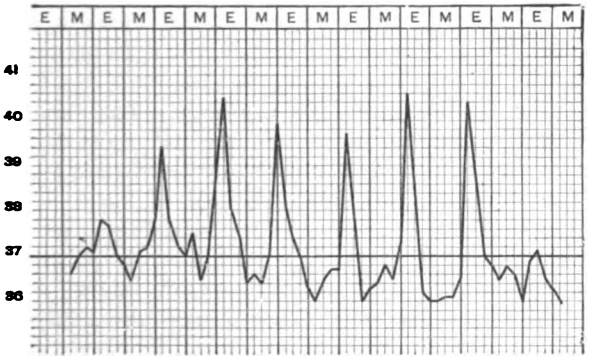


Chart 4.—Quotidian fever (two generations of L. malariæ).

the two benign and the subtertian parasites are generally found associated together, and the latter can be acquired at any time in the tropics, it is only in the summer or early autumn that it can be acquired in the subtropics and more temperate zones. It is stated that if the temperature falls below 15° C. the development of the oöcyst in the mosquito is arrested. On the other hand, when once the sporozoites have entered the salivary glands of the anopheles they are capable of infecting man with the parasite even during the winter season.

Microscopical examinations in subtertian malaria.—In malignant infections developmental forms of the parasite, other than the ring or the crescent, are not usually found in the peripheral blood; when present they indicate a very severe infection. On the occurrence of chilliness or of rigor, and at least during the earlier stages of the paroxysm, many small unpigmented parasites, some-

Digitized by Google

times exhibiting active amœboid movement, sometimes appearing as rings, will be found in finger-blood; but towards the end of the fever these unpigmented forms often diminish in number, and all evidence of parasitic infection may even disappear from the blood till the approach or incidence of the next paroxysm. Of course, crescents and pigmented leucocytes may be found during these temporary absences of the intracorpuscular parasites. The sporulating forms of the malignant parasite are best found by aspirating the spleen with a hypodermic needle—hardly a justifiable procedure, unless in exceptional circumstances.

It must be remembered that in primary attacks of subtertian malaria, even with the most alarming clinical symptoms, parasites may be very scanty in the blood stream, and three or more blood examinations may be necessary for their detection; they may even be altogether absent for the first ten days. This curious fact may be explained by the peculiar location of the organism within the human body.

Clinical forms of subtertian malaria.—The clinical guises which subtertian malaria may assume are most protean in character; it may simulate to a very marked degree many other tropical fevers and even surgical conditions.

REMITTENT TYPES

Bilious remittent.—One type of fever, known as bilious remittent, has long been recognized on account of the bilious vomiting, gastric distress, sometimes bilious diarrhœa, sometimes constipation, which accompany the recurring exacerbations. It is further distinguished by the pronounced icteric or, rather, reddish-yellow or saffron tint of skin and scleræ—a tint derived, probably, not from absorption of bile as in obstructive jaundice, but from modified hæmoglobin (hæmaphein) free in the blood or deposited in the skin and sclerotics. These bilious remittents are very common in the more highly malarious districts of Africa, America, the West Indies, India, and, in fact, in all malarious tropical countries. They are not usually directly dangerous in themselves, but they are apt to result in profound anæmia, and are often but the prelude to chronic malarial saturation, bad health, and invaliding.

Typhoid remittent.—A modification of the bilious remittent—the "typhoid remittent"—is very much more grave, as affecting life, than the simple bilious remittent. In the typhoid remittent, typhoid symptoms—such as low delirium, prostration, dry tongue, swelling of spleen and liver, subsultus tendinum, marked melanæmia

Digitized by Google

—are superadded to the usual symptoms. Though recovery is the rule, a considerable proportion of such attacks prove fatal.

Adynamic remittent.—Some writers class by themselves a set of cases they call "adynamic remittent"—cases which are characterized by fatuousness, restlessness, nervous depression, intense muscular and cardiac debility, profound and rapid blood deterioration, icterus, liability to syncope, occasionally a transient hæmoglobinuria (as was observed in some of the Salonica cases), liability to hæmorrhages, and a marked tendency to local gangrene.

Tuberculosis, syphilis, renal disease, or alcoholism will often be found as factors in determining the two latter types of fever.

PERNICIOUS ATTACKS

Many writers have drawn attention to what are called pernicious attacks or pernicious symptoms—the French neatly designate them "accès pernicieux"—a series of phenomena, the possibility of the appearance of which, not only in the course of remittents but in the course of what is seemingly only an ordinary paroxysm of intermittent fever, should never be lost sight of by the practitioner in tropical climates. These "accès pernicieux" may supervene in apparently mild cases and carry off the patient with horrifying suddenness—as suddenly as an attack of malignant cholera. The wary practitioner is always on the look-out for them, and is always prepared with measures to meet them properly when they threaten.

Pernicious attacks are roughly classified into cerebral and algid. The cerebral are divisible into hyperpyrexial, comatose, convulsive, paretic, and so forth; the algid into syncopal, choleriform, dysenteric, hæmorrhagic, etc.

Cerebral Forms

Hyperpyrexia.—There can be little doubt that many of the cases of sudden death from hyperpyrexia and coma, usually credited to what has been called "ardent fever" or "heat apoplexy," are really malarial. If careful inquiry be made into the antecedents of many of these cases, a history of mild intermittent fever will often be elicited; or it will be found that the patient had been living in some highly malarious locality.

In the course of what seemed to be an ordinary malarial attack the body temperature, instead of stopping at 104° or 105° F., may continue to rise and, passing 107°, rapidly mount to 110° or even to 112°. The patient, after a brief stage of wild maniacal or,

Digitized by Google

perhaps, muttering delirium, becomes rapidly unconscious, then comatose, and dies within a few hours, or perhaps within an hour, of the onset of the pernicious symptoms.

Coma.—Sometimes the patient, without hyperpyrexia, the thermometer perhaps not rising above 104°, or even so high, may lapse into coma. The coma may pass away with crisis of sweating; on the other hand, an asthenic condition may set in and death from collapse supervene.

Other cerebral forms.—Besides these hyperpyretic and comatose conditions, other forms of cerebral attack may occur in the course of malarial fevers. Thus, there may be *sudden delirium* ending in coma and, perhaps, death; *convulsive seizures* of an epileptic or of a tetanic character, with or without delirium or coma—forms especially common in children, and too often misdiagnosed, and with fatal consequences; conditions simulating *cerebro-spinal meningitis; delusional insanity; dementia;* various forms of *apoplectic*-like conditions and of *paralysis*, complicated, it may be, with *aphasia*. Seizures of this description, if not fatal, may eventuate in *permanent psychical disturbances* with a tendency to *suicide*. Temporary debility, or even complete *loss of memory*, may succeed severe malarial infection.

Embolism of cerebral capillaries.—These cerebral attacks are now explained, and, it appears, correctly explained, by the supposition, founded on actual post-mortem observation, that they depend on embolism by malaria parasites of the capillaries of the various nerve-centres involved: in hyperpyrexia, the thermic centres; in aphasia, Broca's convolution. Monoplegia or hemiplegia, and so on, may result by implication of special brain areas. By microscopical examination of properly prepared sections of the brain in fatal cases, such a plugging of the vessels can generally be readily observed. (Plate VI., Fig. 1.)

Malarial amblyopia.—In rare instances a comatose pernicious attack eventuates in blindness. The amblyopia is usually transient, lasting for an hour or two only. On the other hand, it may be persistent; in which case, according to Poncet, optic neuritis, peripapillary œdema, extravasation of leucocytes, plugging of retinal and choroidal vessels by parasites or pigmented leucocytes, and consequent multiple hæmorrhages, may be found in the fundus. If the hæmorrhages are minute they are discoverable by the microscope only. These fundus changes differ from those in quinine amblyopia. In the latter, depending on retinal anæmia from toxic spasm of the arterioles, the amblyopia is more persistent; the discs are white and the vessels shrunken; there are

Digitized by Google

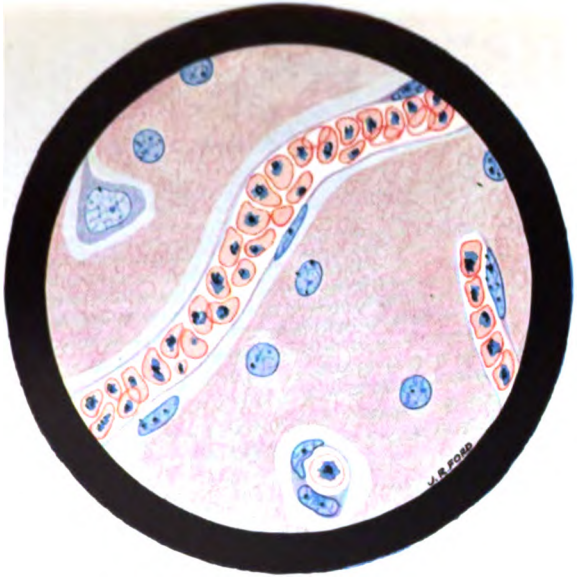


Fig. 1.—Brain section, showing sporulating forms of Laverania malariæ blocking capillaries of cortex. (*Gauducheau's stain.*)

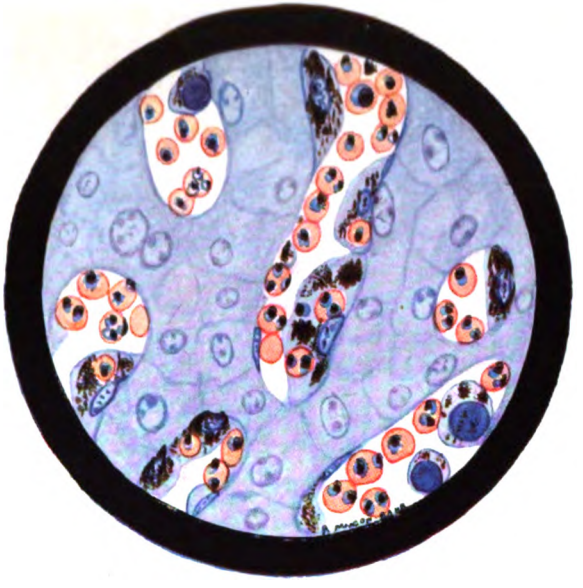


Fig. 2. Liver section, showing phagocytosis of pigment by endothelial cells (Küpffer's cells) and by leucocytes, with large numbers of developing forms of L. malariæ. (*Giemsa's stain.*) (*Orig.*)

SUBTERTIAN MALARIA: SECTIONS OF BRAIN AND LIVER.

PLATE VI.

Digitized by Google

Digitized by Google

no inflammatory symptoms; and central vision is the first to recover.

Amblyopia of malarial origin needs to be distinguished from that produced by overdoses of quinine; in the latter case the onset is sudden, accompanied by deafness, and both fundi are generally affected. An ophthalmoscopic examination shows a white haze over the fundus and a cherry-red spot at the macula; the optic disc is pale and the retinal vessels are markedly constricted (p. 68).

Acute hæmolytic anæmia.—One has observed a rapidly developing and progressive anæmia in the fourth or fifth week of a primary subtertian attack, comparable only to what is seen in the most advanced stages of pernicious anæmia. The clinical features in these cases are characterized by great pallor of mucous membranes and conjunctivæ, cardiac distress and dyspnœa, hæmic murmurs, and retinal hæmorrhages; the blood picture by a blood-count of under 1,000,000, extreme leucopenia, a reduction of hæmoglobin to 10 per cent. or under, the appearance of microcytes and megaloblasts in the blood. The pathology of these conditions indicates the hæmolytic nature of the malaria toxin and its action upon the bone-marrow, which shows megaloblastic response (Fairley and Dew). In consequence of the bone-marrow changes and the inhibition of leucocyte production, sufferers from subtertian malaria are more susceptible to secondary infections of all kinds.

Algid Forms

The algid forms of pernicious attack, as indicated by the name, are characterized by collapse, extreme coldness of the surface of the body, and a tendency to fatal syncope. These symptoms usually coexist with elevated axillary and rectal temperature.

Gastric form.—This may be associated with, and in a measure be dependent on, acute catarrhal dyspeptic trouble. It is accompanied by severe epigastric distress, tender retracted abdomen, and incessant vomiting. The vomited matter may contain blood.

Choleraic form.—Malarial attacks are sometimes accompanied by choleraic symptoms. The stools suddenly become loose, profuse, and numerous. They are not generally so profuse or colourless as the rice-water discharge which pours from the patient in true cholera; they retain a certain amount of biliary colouring, and may be mucoid or even bloody. As in cholera, the serous drain may lead to cramps in the limbs, loss of voice, pinched features, "washerwoman's fingers," almost entire suppression of urine, and perhaps to fatal collapse. Such attacks are very deceptive and

Digitized by Google

may be mistaken for true cholera. The high axillary temperature, if present; a history, maybe, of recent ague fits; the subsequent rapid disappearance of choleraic symptoms on the appearance of the hot and sweating stages; the colour of the stools, and other collateral circumstances, usually suffice for diagnosis, particularly if they are supplemented by a microscopical examination of the blood. Although not usual, recurrence of the choleraic symptoms may take place at the next fever period. This dangerous type of malarial fever was noted in Salonica and Palestine during the War, and is said to be prevalent in the Punjab. Without the microscope its true nature may be hard to recognize.

Dysenteric and hæmorrhagic forms.—Another form of pernicious attack is characterized by the sudden appearance of dysenteric symptoms, by severe and recurring hæmatemesis, or by hæmorrhage from the bowel or elsewhere. The possibility of a suddenly developed hæmorrhage from the bowel of this nature being of malarial origin must therefore be kept in view; particularly if, in what at first sight appears to be ordinary dysentery, the axillary temperature is found to be abnormally high. In every case of this kind, of hæmorrhage from stomach or bowel, in a patient who has recently been exposed to the chance of malarial infection, the possibility of the symptoms being an expression of malarial disease must never be overlooked; an examination of the blood must be made in all such cases before treatment is instituted. It must not be forgotten that subtertian malaria commonly occurs in localities in which either bacillary or amœbic dysentery is also a pathological feature, and that in both of these diseases it forms a dangerous complication.

Hæmorrhages into the mucous membranes of the mouth, and even multiple petechiæ of the skin, have been observed in such cases.

Syncopal form.—In the preceding types of algid pernicious malarial attack the dangerous symptoms mostly show themselves in the rigor stage of the fever. There is yet another form in which the danger appears to depend on an exaggeration of the symptom usually hailed as bringing relief and, for the time, freedom from danger. Thus the sweating of the stage of defervescence may be excessive and cause collapse which, if the patient rise up suddenly or make an undue effort, may lead to fatal syncope. Weak and cachectic patients, therefore, should be warned of this possibility. Death from suddenly developed cardiac failure is common in the pernicious forms of subtertian malaria, and is due to the severe toxic fatty degeneration of the myocardium (Dudgeon and Clarke).

Digitized by Google

The **pathology of the various forms of algidity** is in all likelihood of a very mixed character. In the gastric, choleraic, and hæmorrhagic types there are probably accumulations of parasites in the vessels of the intestinal mucosa, as have been described. In those attacks in which profuse sweating is the dangerous element the diaphoresis may be regarded, at all events in part, as symptomatic of excessive blood destruction —of what is, in reality, equivalent to a sudden and extensive hæmorrhage; or it may be that it is only an excessive reaction to the malarial toxin. The syncope which attends all types of algidity is secondary, and merely an expression of collapse.

A phenomenon occasionally observed in pernicious attacks, especially in those of an algid type, is the flooding of the peripheral blood with vast numbers of parasites, it may be at all stages of development—gametes as well as schizonts. The prognosis in such cases is bad.

Rarer forms of subtertian malaria.—Pulmonary forms have been described with congestion of the pulmonary vessels and bronchitic symptoms. Cases with rapidly developing anasarca and ascites were rarely observed in Macedonia and in Palestine during the War; and, lastly, œdematous forms with nephritic signs, such as the presence of blood-cells in the urine, have been noted. Gangrene of the toes, and disturbances in the vaso-motor mechanism, as in Raynaud's disease, have been observed in subtertian malaria.

Malarial rashes.—Apart from cutaneous petechiæ, an erythema of a pale mauve colour occurring on the sides of the chest and abdomen has been described. The Editor has seen several instances in which this odd appearance was present.

Complications.—Subtertian malaria may complicate, or be complicated by, almost any other disease; a common and very fatal terminal event is pneumonia of either the lobar or broncho-pneumonic variety, noticeable in the influenza epidemic of 1918. When in association with enteric it greatly complicates the clinical picture. The same may be said of the main forms of dysentery. Pulmonary tuberculosis is very prone to supervene in cachectic cases. Apparently the liability to septic infections of all kinds may be explained by the exhaustion of the leucoblastic tissue of the bone-marrow and the absence of any leucocytic response in malarial subjects. Finally, a malarial relapse may take place after any surgical operation, or after parturition, or shock or strain of any description, in a subject previously infected; and the

Digitized by Google

surgeon in the tropics would do well to bear this fact constantly in mind.

A practical experience of these suddenly developed pernicious fevers of the tropics teaches that we should never make light of any malarial attack ; particularly if it be of a mild irregular character and imperfectly controlled by quinine, and if small parasites, or the crescent form, be present. The practitioner should be on the alert for any danger signal—mental aberration, restlessness, tremor, peculiarity in behaviour, alteration in knee reflexes, and other indications of grave implication of the nervous system. It further teaches that the subjects of such fevers should be particularly careful to guard against chills, fatigue, insufficient and unwholesome food, etc.

Differential diagnosis.—There is a natural tendency for medical men inexperienced in tropical diseases, and unacquainted with the vagaries of subtertian malaria, to diagnose the varied symptoms as manifestations of some other disease and even of surgical conditions, such as appendicitis or cholecystitis, demanding operative interference. The following tabulated statement will be found useful :—

(*a*) *Cerebral forms* of subtertian malaria are mistaken for sunstroke, heatstroke, mental derangement, hysteria, aphasia, convulsions, epilepsy, cerebro-spinal meningitis, and even plague.

(*b*) *Abdominal forms*, for dysentery, both amœbic and bacillary, cholera or paracholera, intestinal obstruction, appendicitis, cholecystitis, hæmorrhagic pancreatitis, and liver abscess.

(*c*) *Pulmonary forms*—i.e. malarial pyrexia with pulmonary congestion and myocarditis—for bronchitis, pneumonia, and pleurisy, especially on the left side (due to congestion of spleen), disordered action and even valvular disease of the heart.

(*d*) Those with *cutaneous petechiæ*, for measles, endocarditis, or purpura.

(*e*) The *febrile* cases with remittent pyrexia, for influenza, rheumatic fever, enteric, phlebotomus fever, trench fever, influenza, paratyphoid and relapsing fever.

(*f*) The *icteric* cases, for yellow fever, Weil's disease, or febrile obstructive jaundice.

(*g*) The *cachectic* cases, for acute nephritis, pernicious anæmia, spleno-medullary leucocythæmia and debility, or even pulmonary tuberculosis.

Digitized by Google

Morbid Anatomy and Pathology of Malaria

The blood.—As the malaria parasite is a blood parasite, we naturally expect that the primary effect of its presence will be exercised on, and manifested in, the blood; and as the parasite lives in and at the expense of the corpuscles, destroying a certain proportion of them—in fact, all those attacked—we look, in the first instance, for a corresponding diminution in the number of the corpuscles—an oligocythæmia.

In order to produce symptoms, it is estimated that there must be at least one parasite to every 100,000 red cells.

Oligocythæmia.—The reduction of the red cells in malaria cannot be accounted for by the proportion of the red blood-corpuscles attacked or directly consumed by the parasite. The amount of hæmolysis actually produced by the mechanical action of the parasites should be easily compensated by the latent physiological hæmogenic margin, but this is not the case.

Often, after a single paroxysm of some pernicious malarial fever, as many as half a million or even one million corpuscles per c.mm. drop out of the normal five millions; and this reduction may go on, as paroxysm follows paroxysm, until the corpuscular richness has fallen to one million, or even less. Malarial oligocythæmia is accompanied by changes in the red cells themselves, such as poikilocytosis, basophilic stippling, and other signs of degeneration of the red cells.

Leucocytes in malaria.—The work of many observers tends to show that the leucocytes are increased during the actual malarial paroxysm, and subsequently become diminished. After the malarial attack they again become normal, or there may be a relatively small leucocytosis with an increase of the large mononuclear cells above 15 per cent. The greatest increase of these cells is during the apyrexial periods.

Diminished hæmoglobin value of corpuscles.—In addition to the destruction of the red cells there is a marked hæmoglobin diminution of the surviving corpuscles to 10, 20, or even 50 per cent.

Size and shape of the blood-corpuscles.—On the whole, in malaria, as in most anæmic conditions, the corpuscles are larger than normal—particularly those attacked by the parasite, especially the tertian parasite. Occasionally we come across genuine megalocytes and, not infrequently, certain very minute, darkly coloured spherical corpuscles, which may be nucleated and of embryonic type. Erythrocytes with basophilic stippling are not uncommon, and most

Digitized by Google

pathologists regard these basophilic granules as evidence of the degeneration of the erythrocytes.

Diminished amount of blood.—In all malarial conditions of considerable standing there is a marked diminution in the volume of the blood; we do not, therefore, at the post-mortem examination find that congestion of the organs which is so marked a feature of most specific fevers.

Macroscopic morbid anatomy.—The *spleen* is enlarged—often very much enlarged; its surface is dark—black sometimes—what is called pigmented. On section, the gland tissue is also found to be dark. Generally the parenchyma of the organ is so much softened as to be almost diffluent, so that the tarry pulp can sometimes be washed away by quite a gentle stream of water. The *liver*, too, is softened, congested, enlarged, and pigmented, and of an olive-brown colour. The vessels of the *pia mater* and *brain cortex* are full, and the grey matter may present a peculiar leaden hue. The *marrow* of the spongy bones, such as the sternum and the bodies of the vertebræ, is also dark and congested; and a similar state of pigmentation and perhaps congestion may be discovered in the *lungs*, *alimentary canal*, and *kidneys*.

Microscopic.—*Malarial pigmentation* may be found in blood from any of the organs previously mentioned, within the endothelial cells of the arterioles and capillaries, as minute grains or actual blocks; it may be aggregated so as to form veritable thrombi and occlude vessels (Plate VI., Fig. 2). In the solid organ the pigment, as well as developmental and segmenting forms of the subtertian parasite, is often found ingested by inflammatory macrophage endothelial cells. Particularly is this the case with the spleen and bone-marrow; often, too, with the brain, liver, epiploön, and intestinal mucosa. The spleen and bone-marrow are further distinguished from the other organs mentioned by the position in which the hæmozoin occurs in them. In all organs the pigment is found in the blood-vessels, but only in these two organs is it found in the cells of the parenchyma as well, and outside and away from the blood-vessels. In the liver it is found in the interstitial or Küpffer cells.

Nature and source of malarial pigment.—The pigment is identical with that formed within the malaria parasites and is insoluble even in strong acids; it is altered by potash and is entirely and rapidly dissolved by ammonium sulphide. In recent infections it occurs as minute dust-like grains; in infections of some standing as coarser particles, or as agglomerations of these into irregular, mamillated lumps. It is an iron-containing derivative of hæmoglobin which

Digitized by Google

is primarily split up into a proteid globin and a pigment—hæmatin, and it is from the latter that hæmozoin is derived.* This pigment in the solid organs is apparently carried to these situations by the large mononuclear, and even the polymorphonuclear leucocytes; one can sometimes observe the ingestion of this material in fresh preparations made from the peripheral blood. So far as the circulation is concerned, such a pigment is found in no other disease whatever. As an extravascular pathological product a similar pigment is found in schistosomiasis and certain melanotic tumours; but only in the cells of the tumour, never in the blood-vessels.

Blood of the splenic vein and liver.—Of all the vessels of the body the splenic vein is that in which malarial pigment is most abundant. Whereas in other vessels it is found to be included in ordinary leucocytes, in this vessel it is included in large white cells, probably identical with splenic pulp cells. The reason for this is that the spleen is not only the physiological destination of the hæmozoin-laden leucocytes, but is also a favourite nursery of the parasite.

The yellow pigment.—Besides the pathognomonic black pigment (hæmozoin) there is usually found in the organs a greater or less amount of a yellow or brown pigment (hæmosiderin), the "pigment ochre" of Kelsch and Kiener. This pigment is found not only in the capillaries, but also, and in greatest abundance, in the parenchyma cells of the liver, spleen, pancreas, kidney, as well as in the bone-marrow and in the connective tissues. It is not characteristic of malaria, but occurs in all morbid processes in which there is extensive breaking-up of erythrocytes, as in paroxysmal hæmoglobinuria, in pernicious anæmia, in organic poisoning, etc. It is equally insoluble in acids, in alkalis, and in alcohol. At first, when freshly deposited, it gives no evidence, under the usual micro-chemical tests, of containing iron; after it has been in the tissues for some time it appears to be altered in character in this respect, and it then gives a ferrous reaction with ammonium sulphide and with the double cyanide of iron and potassium. It is a derivative of hæmatin, which splits up into hæmatoidin and hæmosiderin.

Polycholia and hæmoglobinæmia.—Under ordinary conditions of physiological waste the products of the effete blood-corpuscles are converted into bile pigment, and so got rid of. Up to a certain degree of pathological hæmoglobinæmia the liver can deal in a similar way with the free hæmoglobin; so it comes about that, when this substance is free in the blood in unusual abundance,

* Recently Wade Brown has suggested that hæmozoin and hæmatin are identical.

Digitized by Google

the secretion and flow of bile become correspondingly increased. If this flow of bile be excessive it gives rise to what are called " bilious symptoms "—bilious vomiting, bilious diarrhœa—symptoms which are so common in malarial disease, particularly in that variety known as " bilious remittent." Thus, polycholia is a constant and often urgent feature in most malarial fevers, and is good evidence that in malarial infections there is a surcharge of the blood with free hæmoglobin. It is not improbable, although this point is disputed, that the yellowness of the skin and scleræ observed in these fevers is due to tinting by free hæmoglobin, to a hæmoglobinæmia in fact, and not, as is popularly believed, to biliousness or cholæmia from bile absorption.

The yellow pigment is deposited in excessive hæmoglobinæmia.—As in those other conditions referred to as being attended by rapid hæmolysis, in severe malarial fevers in which there is great and sudden liberation of hæmoglobin which the liver cannot at once deal with, the liberated hæmoglobin, pending its transformation into bile pigment, is taken up by the protoplasm of the cells of the different tissues and organs of the body and precipitated in them in a slightly altered form ; it is stored up, in fact, waiting to be worked off as bile pigment by the, for the time being, overtaxed liver. The yellow pigment is, in all probability, this precipitated hæmoglobin.

Great access of hæmoglobinæmia results in hæmoglobinuria.—Should the liberation of hæmoglobin go beyond this, be too great and too suddenly effected for the excretory powers of the liver and the storage capacity of the tissues, then the hæmoglobin, little altered in composition, seeks a more speedy way of escape by the kidneys, and hæmoglobinuria is produced. This is what is found in ordinary paroxysmal hæmoglobinuria and in toxic hæmoglobinuria ; and in this way we may account for the peculiar features of the disease to be described later on—hæmoglobinuric or blackwater fever.

The cause of fever and of periodicity in malaria.—The cause of fever in malaria is some toxin or toxins liberated when the segmented parasites break up in the blood. Rosenau and others, by injecting filtered blood-serum procured during the cold stage of an ague, have succeeded in demonstrating the presence in the blood of such a substance.

The cause of the periodicity is doubtless of a twofold character, the first and most important being the more or less fixed life-span of the parasites, and the second some physiological property in the human body which tends to destroy the parasites. Like so many physiological phenomena, this malaria-destroying principle or

Digitized by Google

force has a tendency to quotidian increase and decrease. Although sometimes almost powerless to cope with the parasites, it usually brings about, especially after repeated infections, a more or less complete immunity.

Malarial Cachexia

Malarial cachexia is the term applied to a group of conditions, more or less chronic, believed to be the result of an antecedent attack of severe malarial fever, or of a succession of such attacks, or of prolonged exposure to malarial influences.

Undoubtedly many of the more or less chronic morbid conditions which were formerly attributed to the malaria parasites are the outcome of infections by trypanosomes, by the Leishman body, by spirochætes, by filariæ, by schistosomes, or by some as yet unidentified protozoal organisms.

The leading symptoms are those of anæmia, characterized by the peculiar sallowness of the skin, yellow sclerotics, enlargement of the spleen and, it may be, of the liver as well; as a rule, the subjects of cachexia are liable to frequent and irregular attacks of fever, though in highly malarious countries it is not unusual to see cases in which fever has never been a feature, or it may have been very mild in character. In such countries a large proportion of the population have enormously enlarged spleens, causing great protrusion of the abdomen, together with much emaciation and dry, rough skins. It is said that in some intensely malarial countries children are occasionally born with enlarged spleens; in rare instances they are infected through the mother in utero, but it is probable that in most cases they become inoculated with parasites immediately after birth.

In the young the general growth of the body is stunted and puberty retarded, and abortion and sterility are common effects of malarial cachexia in adults.

It would seem that the body can become accustomed to the fever-producing toxin of the malaria parasite, much in the same way as it may become accustomed to opium and many other organic poisons, so that a benign tertian parasite, for instance, can undergo a rhythmical development in the blood without the production of an ague attack or other subjective symptoms.

A variety of functional troubles, often observing a curious periodicity, is met with in malarial cachectics; thus one may observe quotidian or tertian neuralgias, gastralgias, vomiting, headaches, tachycardia, and so forth.

Digitized by Google

There is considerable doubt whether a peripheral neuritis of malarial origin exists. Undoubtedly, well-marked neuritis is met with in certain patients, especially from the West Coast of Africa, though it is possible that cachectic and anæmic subjects are much more prone to contract specific infections of all kinds, of which peripheral neuritis may be one.

Herpetic eruptions are very common in malarial cachectics, and so are hæmorrhages of various kinds, such as epistaxis, hæmoptysis, hæmatemesis, melæna, and purpura. In such patients trifling operations—a tooth extraction, for instance—may prove to be dangerous. Subjects of a malarial cachexia are liable to suffer from intestinal irregularities of all kinds.

Splenic enlargement.—The spleen may become so enlarged under repeated attacks of the congestion attending a succession of fever fits, or in consequence of a less active and perhaps feverless hæmolysis, that it may come to weigh many pounds, and so to increase in bulk as to occupy nearly the entire abdomen. The capsule of the gland, particularly on its convex surface, is thickened, and perhaps the seat of fibrous patches, or even of adhesions to neighbouring organs. Many of the trabeculæ forming the framework of the gland become greatly hypertrophied. On section, the tissues of such a spleen are found to be moderately firm, and usually of a reddish-brown colour; but when death happens soon after or during a febrile attack, the section of the gland shows a dark surface from deposit of hæmozoin, the pulp at the same time being softened. Perhaps from over-distension some of the vessels in the interior of the gland give way, and then there is a breaking-down of the spleen pulp in patches, the remains of splenic tissue floating about in the extravasated blood.

"Splenic index."—There are practical points in connection with malarial spleen which deserve mention. The relative absence, or prevalence, of these enlarged spleens or "ague cakes" in the native population is an excellent rough indication of the salubrity or the reverse, as regards malaria, of any particular district. Wherever they are common the district is malarious, and therefore unhealthy, perhaps to Europeans deadly, and should be looked upon as extremely unfavourable for either camping or residential purposes.

Another practical point is that these enlarged spleens are easily ruptured by a blow on the belly; this fact must be remembered in administering even mild corporal punishment to natives of malarious countries. Splenic ruptures are, of course, unless immediately operated on, generally fatal. Occasionally the spleen may rupture

Digitized by Google

spontaneously owing to accession in size in the course of an attack of fever.

Changes in the liver.—Like the spleen, the liver in malarial cachectics becomes enlarged during accessions of fever. Under the influence of a succession of acute attacks, hepatic congestion may gradually acquire a more or less permanent character.

It is in livers of this description that a form of what is called *siderosis* is produced—a condition resulting from chemical changes undergone by the yellow pigment with which the various cells of the organ are charged. It has already been stated that, when first deposited, this pigment gives no ferrous reaction with ammonium sulphide, or with the double cyanide of iron and potassium; and that, as the deposit becomes older, chemical changes ensue, resulting in the elaboration of a form of iron which will then yield the characteristic black colour with the former, and blue colour with the latter reagent.

Certain clinical facts about malarial hepatic congestion and hepatitis are of importance. In the first place, such conditions do not tend to terminate in suppuration; in the second, they are almost invariably associated with splenic enlargement. These are important facts to recollect when it becomes a question of the diagnosis of malarial hepatitis from abscess of the liver. Another important fact to remember is that recent malarial enlargement of the liver is usually curable, depending, as a rule, on simple congestion; whereas old-standing malarial hepatic enlargement is usually incurable, depending, as it usually does, on hypertrophy of the connective tissue and a cirrhotic condition of the organ.

Changes in the kidneys and the heart.—Changes similar to those found in the liver in the course of, and in consequence of, malarial disease occur in the kidney; in time they result in confirmed Bright's disease. Hence, probably, the frequency of Bright's disease in some highly malarious climates. As a consequence of defective nutrition from prolonged anæmia and recurring fever, the muscular tissue of the heart in chronic malarials may degenerate, the ventricles dilate, and, in time, the lower extremities become œdematous. For the same reason the subjects of valvular affections of the heart, whether compensated or otherwise, must be regarded as unsuitable for residence in malarial countries.

Digitized by Google

CHAPTER III

EPIDEMIOLOGY AND ENDEMIOLOGY OF MALARIA

In considering the epidemiology of malaria two things must be carefully distinguished: (1) the circumstances leading to the invasion of the human body by the malaria parasite; (2) the circumstances determining the clinical manifestation of such invasion.

Circumstances favouring Infection

In the mosquito-malaria theory, now thoroughly established, we have the key to this problem. Whatever favours the presence and increase of the malaria-bearing species of mosquito tends to the increase of malaria, and vice versa; whatever favours the access of these insects, and the parasites which have passed into them, to the human body favours the acquisition of malaria.

Geographical range.—The geographical range of malaria is very great; it extends in the northern hemisphere from the Arctic Circle to the Equator, and in the southern probably as widely. Malaria is not uniformly distributed throughout this vast area. It occurs in limited endemic foci which tend, speaking generally, to be more numerous and larger as the Equator is approached.

Influence of latitude and season.—In colder latitudes the association of malaria with swamps is marked; in warmer latitudes this association is much less apparent. In colder latitudes the type of disease is milder; in warmer latitudes it is apt to be more severe. In certain warm countries, as the Argentine, Barbadoes, and many of the islands of the South Pacific, malaria is entirely absent. In colder latitudes it is active only during the summer or early autumn; in warmer latitudes it is perennial, certain seasons —usually, though not invariably, the warmer, or after the rains —being the more malarial.

Influence of local conditions.—The strip of flat, waterlogged country lying along the foot of mountain ranges, the deltas of large rivers, the pool-dotted beds of dried-up streams, areas of country which have fallen out of cultivation, recently deforested lands, are, in many instances, notoriously malarial. Well-drained uplands and carefully cultivated districts are, as a rule, healthy. There are, nevertheless, instances of elevated, arid, and sandy

Digitized by Google

plains which, under certain hydraulic conditions, are intensely malarial. Towns are much less malarial than villages or the open country.

Endemic and epidemic fluctuations.—From time to time malaria extends beyond its endemic foci, spreading in epidemic form over large tracts of what is usually healthy country. There are a few well-authenticated instances of countries (Mauritius, Réunion) which, although previously exempt, subsequently became epidemically malarial; and there are many instances of countries previously malarial which afterwards, especially under the influence of cultivation and drainage, became salubrious.

These circumstances evidently have reference to the distribution of species of malarial mosquitoes. Like other insects, mosquitoes occasionally, under specially favourable conditions, increase enormously in numbers and spread out in every direction. New species, which may belong to the malaria-bearing kinds, may be introduced into places where they formerly did not exist, just as *Culex fatigans* has been introduced into Australia. It is believed that a mosquito capable of subserving the malaria parasite was introduced in this way in the early 'sixties into Mauritius, an island whose fauna and flora had been hitherto very peculiar and special. In this way we can account for the outbreak of the great epidemic of malaria that swept over that formerly healthy island, and also for its present endemic insalubrity. A similar misfortune may very well happen to the non-malarious South Pacific islands in the near future.

The exemption of certain islands from malaria, even though in the midst of an archipelago of malaria-haunted islands, is a very remarkable circumstance. Barbadoes is an instance in point. Low has confirmed the popular belief that malaria is unknown there as an indigenous disease, and points to the absence of Anophelinæ as the explanation. But how explain the absence of Anophelinæ, seeing that Culex abounds and all the conditions favouring mosquito life are present?

Still more remarkable is the circumstance that there are villages and districts in India, as pointed out by Christophers and Stephens, and similar districts in Italy, as pointed out by Celli, in which, though surrounded by highly malarious country and though Anophelinæ abound, there is no malaria. The explanation of this anomaly is not apparent. Perhaps in these places there is some local substance on which the mosquitoes feed that is fatal to the parasite. Sambon ingeniously suggests that there may be special local conditions that favour *hyperparasitism*, that is, the attack and destruction of the malaria parasite by some other kind of

Digitized by Google

parasite. Similar occurrences are common enough in nature. In support of this view he cites Ross's observation of what he designated "*black spores*" (Fig. 21), bodies which are now known to be protozoal organisms belonging to the genus Nosema. These "black spores" prey on the malaria oöcyst in the wall of the mosquito's stomach and destroy it, just as they prey on the larvæ of *Filaria immitis* encysted within the Malpighian tubes of the mosquitoes which subserve their development. Whatever the explanation of the salubrity of these mosquito-haunted plains be, it is well worth searching for; it may be that it would carry a hint of value in attempting the prevention of malaria.

Atmospheric temperature.—One of the most important conditions necessary to the sporogonic phase of the malaria germ is a sustained average temperature of at least 60° F. The malaria parasite will not develop in the mosquito at low temperatures.

Fig. 21.—Ruptured oöcyst containing Ross's "black spores." (*After Grassi.*)

Altitude.—Altitude *per se* has, apparently, no influence on malaria. It is the decrease in temperature, usually implied by an increase in altitude, that is the real determining circumstance in bringing about a diminution in the prevalence of malaria in uplands. In the tropics an elevation of six or seven thousand feet may not secure immunity from malaria unless there be, at the same time, a corresponding and sufficient lowering of temperature. In Italy there are many malarious spots high up among the hills; the same is the case in India and elsewhere in those elevated valleys which are also narrow, imperfectly ventilated, and imperfectly drained.

Moisture.—Another important condition for the production of malaria is the presence of water. In the Sahara there is no malaria unless in the oases; in many of these it is rife—in Biskra, for example. A large expanse of water is not favourable to malaria. The mosquito thrives best in sluggish streams with grassy banks and many backwaters; still better, in small pools or other collections of water, as in broken bottles, empty tins, etc., where there are no fish to prey on their larvæ, and where the surface is not agitated by winds. One such puddle near a house may suffice to render that house unhealthy. As a general rule, the Anophelinæ will not breed in foul or muddy water. Clear pools, as found in many desert oases, with a plentiful supply of green algæ, are their favourite haunts.

Influence of winds and atmospheric diffusion.—It is very

Digitized by Google

doubtful whether the malarial mosquito can be transported very far from its native pool. The mosquito does not ascend more than a few feet from the ground, and in high winds, or even in draughts of air such as that from a punkah, immediately seeks shelter. It is certain that some thousand or fifteen hundred yards of water between a ship and a malarious coast may suffice to secure immunity to the crew. The experience of the notorious Walcheren Expedition proves this. About three miles on land from a malaria source is probably approximately as effective. The diffusion of malaria by winds is generally extremely restricted. Inside a city may be quite healthy, while outside the walls the country may be pestilential. One village may be sickly, whilst a neighbouring village may be healthy. It seems safe, therefore, to conclude that the horizontal and vertical diffusion of the malaria germ—that is to say, of the mosquito—is, as a rule, very restricted.

Influence of trees, houses, and lodging.—The intervention of a belt of trees between a malarial swamp and a village is said to protect from malaria the houses on the leeward side of the trees. The trees may filter out the mosquitoes by affording them protection from winds. Open windows and doors, by giving access to mosquitoes, are sources of danger in malarial countries; for this and similar reasons, sleeping on the ground, on the ground floor, or unprotected by a mosquito-curtain, is dangerous.

Time of day in relation to infection.—Evidently in conformity with the habits of the mosquito, the time just before sunrise and just after sunset, and the night, have the reputation of being the most dangerous as regards liability to contract the infection. Although mosquitoes are most active during twilight and night, they bite readily enough during the daytime in shady and windless places, as in thick jungle or in a dark room. A very few species are diurnal in habit.

Disturbance of the soil.—It has often been observed that in malarious countries, so long as the soil remains undisturbed, agues and the severer forms of fever are comparatively rare; but so soon as building, road-making, and other operations implying soil disturbance commence, then severe malarial fevers appear. After a time when, in the progress of events, these operations have concluded, and the broken surface of the soil has, so to speak, skinned over again, the place becomes once more comparatively healthy. Soil disturbance usually implies the formation of holes. Holes imply puddles, and puddles imply mosquitoes. Workmen from

Digitized by Google

many districts, some of them malarious, are assembled in crowded lodgings; one infected workman suffices to start the epidemic. In the present state of knowledge this seems to be adequate explanation of the recognized danger of earth-cutting in malarious districts.

Circumstances favouring the Clinical Manifestation of Malarial Invasion

As a rule, a successful malarial infection declares itself within a week or ten days. As with other infections, certain individuals resist the pathogenic influences of the malaria parasite for a longer period. A very few appear to be permanently immune. Everything tending to cause physiological depression favours susceptibility and acute manifestations.

Influence of meteorological conditions on relapse.—A malarial subject while in the mild climate of the tropics may keep in fair health; but when, as is so often the case with sailors and others returning to Europe, he is plunged into the stormy winter of the North, is exposed to cold, and has long watches and fatiguing work, very probably latent malaria will become active and ague follow. This is a common experience with malarials from the tropics. It is almost the rule with people coming from the West Coast of Africa.

Study of the mosquito indispensable.—Full knowledge of all that concerns the etiology of the disease will only be attained when we have full knowledge of the various species of mosquito capable of subserving the parasite, and it may be that certain species of Anopheles act as selective intermediaries for the several species of malaria parasites.

Acclimatization and Immunity

Personal acclimatization.—Is there such a thing as acquired immunity as regards malaria? It is a well-established fact that the negro in Africa, although he does get fever, does not get it so frequently nor so severely as the European; even although the latter, from his hygienic ways of living, is of the two much the less exposed to infection. It has been shown that the natives of malarious districts acquire their immunity from repeated and persistent infection in childhood. In such places the blood of practically every child up to three or four years of age contains malaria parasites. The proportion of infected children gradually becomes smaller with each additional year until adolescence is approached, when the blood becomes practically parasite-free and immunity is established.

Digitized by Google

The mortality in native children from malaria is very great; but it would appear that a relative tolerance is soon acquired, for although the negro child may have a rich infection of parasites in its blood, possibly in consequence partly of increasing immunity, partly of some racial and inherited quality, it may exhibit a remarkable tolerance of the malaria toxins. It has often been remarked that these dark-skinned children, with enormous spleens and a rich stock of malaria parasites in the blood, run about fever-free, and apparently in rude health.

Digitized by Google

CHAPTER IV

DIAGNOSIS, TREATMENT, AND PROPHYLAXIS OF MALARIA

Diagnosis

There is a marked tendency to regard and diagnose all fevers occurring in tropical countries, or in individuals who have returned from tropical countries, as malarial. Such slovenliness in diagnosis must be strenuously avoided by the practitioner. It is apt to become a habit which, sooner or later, is bound to have disastrous consequences.

At the same time, the opposite error of overlooking malarial infection must be equally guarded against. In many tropical and subtropical localities practically every European is, or may be, the subject of active or latent malaria. *The tropical practitioner therefore should approach the diagnosis of all his cases, no matter what, with the idea ever present to his mind that they may be malarial or complicated with malaria.*

The three pathognomonic signs of malaria.—These are —periodicity ; the effect of quinine ; the presence of the malaria parasite.

The diagnosis of malarial disease, if all the means at our disposal be employed, is usually not a difficult matter. Formerly, periodicity and the effect of quinine were the tests principally relied on. In certain circumstances they are fallible. Nowadays, in all doubtful and serious cases, it behoves the practitioner to have recourse to the least fallible test—the microscopical examination of the blood. When such an examination yields a positive result, when the parasite in any of its forms, or its characteristic product—hæmozoin—either free in the liquor sanguinis or enclosed in leucocytes, is found, the diagnosis of malaria is securely established. Negative results from a single microscopical examination are not so trustworthy as are positive results ; but if the practitioner has experience, and if he has the opportunity to make his examinations at suitable times and in a case untreated by quinine, they, too, are conclusive, more especially if supplemented by a differential count of the leucocytes.

The quinine test is generally conclusive in intermittents and in

Digitized by Google

the various larval forms of malaria, but the more severe types of remittents are often singularly resistant to the drug. Moreover, time may not be available in which to test such cases with quinine. They may be cases of a threatening nature in which a speedy diagnosis is of the first importance. In such cases the microscope is the only available trustworthy diagnostic agent.

Recent work by Gordon Thomson indicates that a complement-deviation test, using an emulsion of an organ rich in parasites as well as artificial cultures of the plasmodia as antigens, may prove to be a distinct aid to diagnosis.

About 28 per cent. of malarial bloods in the acute stage of the disease give a positive Wassermann reaction; but this is not so in either the chronic or the quiescent stage, and this has to be borne in mind in excluding syphilis in a malarial subject (Fairley).

Periodicity in diagnosis.—Periodicity at times is a trustworthy enough clinical test for malarial disease. *Tertian and quartan periodicity occur only in malarial disease*; when either is thoroughly established, its presence is almost conclusive as to the case being malarial. It is otherwise as regards the significance of quotidian periodicity. Quotidian periodicity we find in greater or less degree in nearly all fevers, particularly in fevers associated with suppuration. In hectic conditions, quite unconnected with malaria, one often sees a quotidian afternoon rigor, followed by hot, dry skin, and a temperature rising even to 103° or 104° F., the febrile movement concluding with a profuse diaphoresis and complete morning apyrexia. Such cases are apt to be misdiagnosed and treated as malarial.

Periodicity of fever in liver abscess: diagnosis from malaria.—Particularly is this the case in suppuration connected with the liver—a condition peculiarly liable to occur in tropical practice. Simulation of malarial fever by hepatic abscess is very common; it is a pitfall into which the inexperienced tropical practitioner often tumbles. In consequence, we find that, at one time or another, most liver-abscess cases are drenched with quinine, on the supposition that the associated fever is malarial. There are several points, even apart from an examination of the blood, which, if duly considered, will avert this blunder.

In hepatic abscess, although the liver is enlarged, the spleen is not necessarily so; splenic enlargement, though an occasional, is not a usual feature in liver abscess. In malarial fever, if the liver be enlarged the spleen is still more so, and usually can be felt extending well beyond the costal margin. In hepatic abscess the fever occurs generally, though not invariably, in the late afternoon

Digitized by Google

or evening; the patient may perspire profusely, independently of fever lysis, at any time of the day or night—very generally whenever he chances to fall asleep. In malarial fever the paroxysm may, and generally does, occur earlier in the day; there is no marked tendency to sweating unless at the defervescence of the fever. In hepatic abscess a history of dysentery is nearly always obtainable if carefully inquired for. If fever be distinctly tertian or quartan in type it is not hepatic. In all doubtful cases the blood must be examined once or oftener, the rigor stage or early hot stage being selected for the examination, and the examination being made before administration of quinine. Apart from the presence or absence of the parasite or of pigmented leucocytes, marked increase of polymorphonuclear leucocytes would be in favour of hepatic abscess; a relative excess of mononuclear leucocytes in favour, though not conclusive, of malaria. Occasionally cases are met with in which there is a history of malarial infection and, in addition to this, a history of dysentery, and the liver and spleen are both enlarged. In such cases diagnosis may be impossible without the microscope and the aspirator.

Diagnosis of bilious remittent from yellow fever. — In bilious remittent the icteric tinting of the skin is an earlier feature; albuminuria is not so common and generally not marked; temperature is maintained high for many days, not subsiding in three or four days as in yellow fever; the vomiting is profuse and bilious; the pulse does not become phenomenally slow as in yellow fever; in the initial stage the eyes are not congested to the same degree; and, of course, the parasite is to be found in the blood.

Diagnosis from other types of paroxysmal fever.—The following also are often mistaken for malarial fever: Cerebro-spinal meningitis; urethral fever; the fever attending the passage of gall-stones, or with inflammation of the gall-bladder; that associated with pyelitis and surgical kidney; lymphangitis, particularly that form of lymphangitis associated with elephantiasis and other filarial diseases; undulant fever; relapsing fever; trypanosomiasis; kala-azar, generally an irregular fever, though often quotidian, and almost invariably attended with enlarged liver and spleen and with anæmia; the fevers associated with tuberculous disease, with ulcerative endocarditis, with some types of pernicious anæmia, with splenic leucocythæmia, especially with visceral syphilis, with rapidly growing sarcoma, with forms of hysteria, and with many obscure and ill-defined conditions. The use of the microscope must not be neglected in such cases if there be the slightest doubt as to their exact nature.

Digitized by Google

It must not be concluded that, although unquestionable evidence of the presence of one or more of the foregoing has been obtained, malaria is absent. Malaria often occurs with these diseases. Malaria is a common complication in trypanosomiasis, for example, and it is often hard to pronounce whether in such cases any given rise of temperature be due to the trypanosome or to the malaria parasite. The same may be said of tuberculosis, of syphilis, and, in fact, of any medical or surgical febrile condition.

Typhoid and paratyphoid fevers.—Without the microscope it is sometimes impossible to diagnose typhoid types of malarial fever from genuine enteric. In both there may be diarrhœa or constipation; in both there may be splenic enlargement; in both there may be typhoid tongue, delirium, and the entire range of typhoid symptoms. As a matter of fact, until quite recent years all typhoid in India was regarded and treated as malarial fever—malarial remittent—and, doubtless, often with disastrous results. In circumstances in which the Widal test or blood culture is available, either is an invaluable supplement to microscopical examination of the blood.

Typho-malarial fever.—One important fact in connection with the diagnosis of typhoid in malaria must ever be kept in mind: in individuals who have previously been subjected to malarial influences and who, perhaps, have suffered at one time from well-marked malarial fever, the oncoming of typhoid is often preceded by three or four paroxysms exactly like those of ordinary ague. This may occur even when the patient has been for some time in a non-malarial country, as England. In such cases quinine is usually given early in the attack: its failure to check the disease should lead to careful prognosis and the avoidance of too active purgation. Similarly, well-marked malaria-like fluctuations of temperature and the appearance of the parasites in the blood in the course of a continued fever do not exclude typhoid. These cases are probably typho-malarial, and have to be treated as such—as typhoid with a malarial complication.

As an outcome of practical experience it is strongly advised that every tropical practitioner should be provided with a travelling microscope, or, at least, should carry about with him a few microscope slides for blood-films. He must be on his guard, however, against concluding from the discovery of malaria parasites in his films that malaria is necessarily the only, or even the principal, disease his patient is suffering from.

Digitized by Google

TREATMENT

Many drugs have been employed in the treatment of malarial disease, and many drugs have some influence on it; all sink into insignificance in comparison with **quinine.** In serious cases, to use any drug to the exclusion of quinine is culpable trifling. Therefore, so soon as a diagnosis of malaria has been arrived at, unless there be some very manifest contraindication, the first duty of the practitioner is to set about giving quinine. There are many ways of exhibiting the drug; however given, care must be taken that it is so administered that there can be no mistake about its being absorbed. If the patient for any reason, such as inability to swallow or persistent vomiting, cannot take quinine by the mouth, and the existing condition is grave, it may be injected per rectum; but if the circumstances of the case are such that neither of these channels for administration is available, and a rapid action of the drug is imperative, it must be injected at once intramuscularly or into a vein.

Treatment of simple benign tertian or quartan attacks.—During a paroxysm of ordinary intermittent fever it is better, before giving quinine, to wait until the rigor and hot stages are over and the patient is beginning to perspire. A fever fit, once begun, cannot be cut short by quinine, and to give quinine during the early stages aggravates the headache and general distress; but so soon as the skin is moist and the temperature begins to fall, the earlier the drug is commenced the better: 10 gr., preferably in solution, should be administered at the commencement of sweating, and thereafter 10 gr. three times a day after meals for the next week, though there appears to be an advantage in giving it, whenever possible, in smaller doses at more frequent intervals—6 doses of 5 gr. each. This is an almost certain cure. The quinine may not always prevent the next succeeding fit, but it nearly always diminishes its severity. In ninety-nine cases out of a hundred the second following attack does not develop.

When giving quinine it is well to administer an aperient and to keep the patient in bed, especially when the liver is congested, the tongue coated, and the alimentary canal contains an excess of mucus; in ordinary cases neither aperient nor rest in bed is absolutely necessary. In cachectics, however, and in all obstinate cases both are valuable adjuvants.

Manson's practice in the treatment of ordinary malarial fevers was to give quinine for a week in the doses mentioned. At the

Digitized by Google

same time, with a view to prevent recurrence of fever, the patient was directed to take, once a week, a mild saline, sulphate of soda or Carlsbad salts, in the morning, and three 5-gr. doses of quinine during the day, or 15 gr. in one dose. After the first week, iron and arsenic in pill, tabloid, or solution, such as a 3-gr. tabloid containing iron hypophosphite, arsenious acid, and strychnine, or a mixture containing ferri et ammon. cit. 10 gr., liq. arsenicalis 3 min., and water 1 fluid oz., are prescribed for a fortnight, and, after an interval of a week, for another fortnight. *The weekly aperient and quinine had better be kept up for six weeks or two months or longer.* In more heavily infected cases one can recommend, after the preliminary week, 5 gr. of quinine daily; this dose to be kept up for three months, and repeated for a month every spring and fall for two years.

The quinine hydrochloride is the form which should be used by preference; it may be obtained in tabloid form, and taken well crushed up in water; the bitter taste is said to be quickly removed by masticating a piece of bread.

Quinine sulphate pills are to be avoided, as they often pass through the intestinal canal without being absorbed. When the sulphate is given in solution it must be dissolved in acid; for instance, 2 min. of the acid. sulph. dil. to every 10 gr. of the salt.

An agreeable and efficacious method of prescribing quinine is to give it in an effervescing mixture composed of 10 gr. of quinine hydrochloride and citric acid mixed together in powder form and added to 20 gr. of ammonium and potassium carbonate with the addition of half an ounce of water. Some consider that the addition of acid. hydrobrom. dil. 30 min. to 10 gr. of quinine obviates the tinnitus.

Dose of quinine: toxic effects.—There is great difference of opinion and practice about the dose of quinine. Some give 30 gr. at a dose, some give 3 gr. The former is too large a dose for ordinary cases, the latter too small. It must never be lost sight of that occasionally quinine in large doses produces alarming effects; not singing in the ears and visual disturbances merely, but actual deafness and even amblyopia, both of which may prove very persistent and occasionally permanent. It may also produce profound cardiac depression and gastric disturbance, and even death from syncope. Urticaria is another, and not very uncommon, effect of even small doses of quinine; some cannot take it on this account, and prefer to endure the disease rather than suffer the intolerable irritation induced by the remedy. The Editor believes that nothing is gained by excessive doses; in

Digitized by Google

ordinary circumstances, 30 gr. spread over two or three days is usually ample to check an ordinary case of benign or quartan malaria.

Quinine amblyopia is generally the result of intense quinine poisoning after a dose of 80–160 gr. In exceptional cases, with an idiosyncrasy to the drug, temporary blindness has followed even moderate doses. Other symptoms, such as mental confusion and coma, may accompany the amblyopia. There is no evidence that a moderate anti-relapse treatment causes permanent injury to the sight, though the field of vision may become contracted.

Quinine in pregnancy.—Care should be exercised in giving quinine to pregnant women, for undoubtedly it sometimes causes miscarriage. The fact of pregnancy, however, must not debar the use of the drug altogether; only, in such circumstances, it should be given in the minimum dose likely to be effectual, say 3 gr. repeated every eight hours for two days. A pregnant woman will run more risk of miscarriage and of detriment to her health from repeated ague fits than from a reasonable dose of quinine.

Quinine in the puerperal state.—It is a wise precaution in malarious countries to give a few 5-gr. doses of quinine during labour or soon after. The puerperal state seems to have the effect, as any other shock or physiological strain might, of waking up the slumbering malaria parasite. A dose or two of quinine in these circumstances does no harm, and may, by choking off a threatening fever, avert suffering and anxiety, not to mention danger.

For children under one year, ½–1 gr. for a dose suffices; for older children the dose must be increased proportionately to age and strength. Children tolerate the drug well, so that in serious cases—pernicious comatose or other cerebral forms—the drug should be vigorously pushed.

If a supposed ague resist the doses of quinine mentioned, the diagnosis should be revised.

Excretion of quinine.—Nierenstein's observations show that the excretion of quinine is the same by whichever route it is administered. The drug appears in the urine within five minutes, and altogether one-tenth of the total quantity is passed in this manner, the highest concentration being 7–11 gr. per litre. The recognition of the drug in the urine is effected by means of the Mayer-Tanret method: 1·35 grm. of mercuric chloride in 75 c.c. of water is mixed with 5 grm. of potassium iodide in 20 c.c. of water in a 100-c.c. flask, the former being poured into the latter solution under agitation. On addition of the urine a turbidity appears if quinine is present.

Other forms of administering quinine.—*Euquinine or*

Digitized by Google

euchinine—the ethyl carbonate of quinine, *quinine tannate*, and *aristoquinine*—a diquinine carbonic ester, have the advantage of being almost tasteless, an important property in the case of fever in children or fanciful patients. All these salts are practically insoluble in water; hence their tastelessness.

McGilchrist, in experimenting with various alkaloids of cinchona, found that *hydroquinine* is about 20 per cent. more efficacious than quinine; but recent research indicates that cinchona bark contains fourteen alkaloids, and of these Acton has shown in a recent publication that the lævorotatory alkaloids—*quinine base* and *hydroquinine*—have a special affinity for the subtertian, while the dextrorotatory alkaloid *quinidine* has a more powerful action on the benign tertian parasite.

Milk as a menstruum for quinine.—If the taste of the ordinary salts of quinine be very much objected to, and if euquinine be not available, a good plan is to give quinine in powder in a tablespoonful of milk after the patient has previously lubricated the mouth with a morsel of bread and butter. Given in this way the bitter taste of the drug is not perceived.

In cases of benign tertian malaria which relapse in spite of quinine treatment—this they are very apt to do, especially in soldiers returning from the East—it is found that continuous dosage with daily small doses of quinine is more efficacious than the irregular exhibition of larger quantities. A great deal can be done by attending to the nutrition, habits, and general health of the patient; this is every bit as important as quinine, and one should always remember to treat the patient as well as to try to exterminate his parasites. Continuous drenching with quinine is of little use in persistent cases; it may be necessary, even in benign malaria, to give a course of intramuscular injections in order to cut the fever short.

Quinine given in this manner is known as anti-relapse treatment. Opinions differ as to the best course to pursue. It may be said that it is advisable to keep up the quinine for three months, either by the so-called week-end system, 30 gr. on each of two consecutive days, or 10 gr. once a day for six days.

Alarming pernicious symptoms supervening in an otherwise straightforward case of benign malaria are usually due to a co-existing malignant infection as well; this is a much more common complication than is generally supposed, and the case must be treated on the lines laid down for the latter type.

Treatment of subtertian malaria.—Mild cases of malaria of the subtertian type due to *Laverania malariæ* may be treated on

Digitized by Google

the same lines as the benign forms, and when the quinine is retained by the mouth and no alarming symptoms supervene, it is advisable to persist on these lines, rather than have recourse to the methods to be described.

Rest is a most important factor. It is undoubtedly true that the malignancy of many cases of subtertian malaria observed in military service is due, to a great extent, to the exigencies of war.

The sooner after infection a case of subtertian malaria is treated by quinine, the more rapid the recovery and the less likelihood of relapse or the development of pernicious symptoms.

In the endemic area of blackwater fever, and in persons who have left that area, large doses of quinine do sometimes undoubtedly determine an explosion of that dangerous disease, especially in the cachectic.

Injection of quinine.—In any type of fever, if vomiting is persistent, if the brain is affected, or if the patient is insensible and cannot or will not swallow, recourse must be had to rectal or intramuscular injection of quinine. In all cases in which life is in imminent danger, and in which the earliest possible action of the drug is of importance, it must be so administered. The *intramuscular* method is sometimes a painful one, and may be attended with some risk; but, in the circumstances, such possibilities count for little. As indications for intramuscular injection, the inefficiency of oral quinine, its non-absorption owing to severe vomiting or gastritis, the presence of severe, toxic, or pernicious symptoms, or of large numbers of parasites in the peripheral blood, may be taken as guides.

The most suitable readily procurable salt for injection* is the

* SOLUBILITY AND EQUIVALENT VALUE OF SALTS OF QUININE

Those marked with an asterisk are suitable for hypodermic injections

Name of salt	Proportion of the alkaloid in the salt	Solubility in cold water	Amount equivalent in value to one of quinine sulphate
Sulphate	73·5 %	In 800 parts	1·00
Hydrochloride	81·8 %	,, 40 ,,	·90
*Bihydrochloride	72·0 %	,, 1 ,,	1·02
Hydrobromide	76·6 %	,, 45 ,,	·96
*Bihydrobromide	60·0 %	,, 7 ,,	1·23
Bisulphate	59·1 %	,, 11 ,,	1·24
Phosphate	76·2 %	,, 420 ,,	·96
Valerianate	73·0 %	,, 110 ,,	1·01
*Lactate	78·2 %	,, 10 ,,	·94
Salicylate	70·1 %	,, 225 ,,	1·05
*Hydrochloro-sulphate ...	74·3 %	,, 2 ,,	·99
Arseniate	69·4 %	Slightly soluble	1·06
Tannate	20·0 %	,, ,,	3·67
*Bihydrochl. of q. and urea	59·2 %	In 1 part	·6

Digitized by Google

hydrochloride or, better, the bihydrochloride, which is soluble in less than its own weight of water. If neither of these salts can be procured the sulphate may be used, solution being effected by adding half its weight of tartaric acid.

In giving an intramuscular injection a stout, preferably platinum-iridium needle should be driven well home, deep into the gluteal muscles, the skin being previously carefully cleansed. The solution must be freshly prepared and boiled, and the syringe and needle thoroughly sterilized. A syringe having a well-fitting glass piston and a plugging needle is the best instrument for giving these injections.

The bihydrochloride of quinine may now be obtained in 5-gr. tabloids, specially prepared for intramuscular injection. Ampoules containing 6 gr. of quinine bihydrochloride to the c.c. of saline are now put on the market. One of these injections may be given into each buttock, and repeated every day for three consecutive days.

When large numbers of intramuscular injections have to be given the quinine solution may be put up in vaccine bottles fitted with a sterilized rubber cap in a solution of 6 gr. of quinine hydrochloride dissolved in 1 c.c. of a 0·75-per-cent. saline. The cap is disinfected and the needle of the syringe plunged through it into the bottle.

The best place for an intramuscular quinine injection is the gluteus maximus muscle at a point somewhere from 2 to 3 in. below the crest of the ilium. After the injection is made the part should be gently massaged so as to diffuse the solution, and the little wound sealed with collodion. *Quinine ought never to be injected into the neighbourhood of large nerves or blood-vessels or impinge upon the bone.* It is a general belief that abscess, indurations, and similar accidents are for the most part attributable to imperfect methods and carelessness.

It has been shown that a concentrated solution of quinine is rapidly absorbed from the tissues, and that its action upon the parasites in the circulation is almost instantaneous. There appears to be no special purpose in further diluting the quinine for the intramuscular route.

Precautions.—It may be well to mention—not with the idea of deterring the practitioner from using the drug in this way, but to impress upon him the necessity for sterilizing the patient's skin at the place selected for injection, and for care in keeping instruments and solutions aseptic—that not only abscess, sloughing, and chronic painful indurations have some-

Digitized by Google

times followed the intramuscular injection of quinine, but also tetanus.

From observations at autopsy it would appear that three intramuscular injections of 12 gr. each, on three separate consecutive days, not only banish all the parasites from the circulation, but also cause a marked alteration in the condition and size of the spleen. There appears to be no necessity for continuous intramuscular injection after the temperature has fallen to normal and the parasites have disappeared; the effect would be to encourage an extensive necrosis of the tissues. When the sulphate is used for injection it is not invariably absorbed; there is evidence to show that sometimes it is precipitated.

Every practitioner should remember that, although the therapeutic effects of intramuscular quinine are indisputable, yet a localized necrosis of the muscular fibres of the gluteus occurs after every injection; this is followed by œdema and, it may be, a destruction of the blood-vessels, thus rendering the muscle a suitable culture-ground for the tetanus or other organisms. The main point to remember is that this method has its *uses* as well as its *abuses*. There is no advantage in repeating the injection day after day in approximately the same spot; if this is persisted in, the most extensive necrosis and hæmorrhages may result. In addition to tetanus and abscess formation, gas gangrene and general streptococcal septicæmia have been observed. Injection into or near the great sciatic nerve has resulted in paralysis of one leg.

Our personal opinion is that these intramuscular injections of quinine in the dosage advocated are quite sufficient to tide over the pernicious symptoms of malignant malaria and to save the patient's life. Continued pyrexia does not necessarily indicate that parasites are still active in the tissues; one should recognize that there is such a thing as malarial toxæmia, for which quinine is useless.

Subcutaneous quinine, as a routine measure, had been largely abandoned, owing to risk of superficial necrosis, but during the Great War it was practised by the French in Macedonia and by ourselves in East Africa, apparently with good results. The dosage is 6 gr. to 1 c.c. of saline; either the hydrochloride or bihydrochloride may be used. The injection is given into the flanks, and is followed by massage with carbolic oil.

Quinine by enema.—Quinine may also be given by enema in those cases in which the symptoms are not severe enough to warrant the prolonged use of intramuscular injection. It is readily absorbed if the bowel be not too irritable. The dose should be a large one, 30 gr. Given in this way, and repeated in an hour or two, in malarial

Digitized by Google

comatose fever, it has sometimes a rapid effect. It is the most effective method of exhibiting the drug in such attacks in children; 5 gr. in warm solution, repeated hourly, retention being ensured by the attendant keeping the patient's buttocks together, is strongly recommended.

Intravenous injection of quinine.—In pernicious cases, in which it is of importance to obtain a rapid and powerful action of the drug, the intravenous injection must be given. The bihydrochloride salt should be used in a dosage of 10–15 gr., dissolved in 10 c.c. of normal saline. In algid or collapsed cases it may be advisable to add more saline, though in comatose ones it does not appear to be of any distinct advantage and may intensify the subsequent reaction. The solution should be boiled in a test-tube before use, and drawn up in a sterile syringe and injected into the median basilic vein, rendered prominent by means of a rubber band. On its introduction into the vein the plunger of the syringe should be slightly withdrawn to observe the entrance of blood into the barrel. The injection should then be made slowly, and at least three minutes spent over the operation. One dose of 15 gr. is usually sufficient to stop the fever and cause the disappearance of most of the parasites within twenty-four hours. If symptoms persist, a second injection may be given a few hours later. Although much larger doses than the one here advocated were given, with apparent benefit, in Salonica, there appears to be no special advantage in pushing the drug to such an extreme degree.

One word of warning based on personal experience is necessary. Occasionally, from the cyanosis and respiratory distress, it can be inferred that the myocardium is severely involved, and in these cases it is necessary to stay one's hand. The amount of toxin liberated by the rapid destruction of the parasites after intravenous injection may be sufficient completely to paralyse the cardiac mechanism, and death may rapidly ensue. It would be much more advisable in cases of this description to give a preliminary intramuscular injection of quinine, and to follow it up six or eight hours later by a small intravenous injection (6 gr.). It is possible that more frequently repeated 3-gr. intravenous doses are more efficacious than are larger ones given at longer intervals.

Other measures.—In the case of coma or convulsions, one should also take into account the fact that a considerable œdema of the brain and increase of cerebro-spinal fluid have been demonstrated in fatal cases in which no sporulating parasites could be found in the cerebral capillaries. In comatose cases which do not clear up

Digitized by Google

after intravenous injection, lumbar puncture and withdrawal of 20 c.c. or so of cerebro-spinal fluid may give great relief. In cases with extensive hæmolysis and in which the parasite has disappeared from the blood, the injection of one or two pints of normal saline solution, as in blackwater fever, has been followed by good results.

In algid cases the intramuscular or intravenous injection of adrenalin (5 min. of a 1-in-1,000 solution) has been advocated.

Warburg's tincture. — A very effective medium for giving quinine, and one of high repute in many places, is Warburg's tincture. This contains, besides quinine, a number of drugs, many of them doubtless inert, although some of them certainly possess valuable therapeutic properties. Experience has shown that the combination is really a good one, and that Warburg's tincture sometimes succeeds where quinine alone fails, or acts too slowly. It generally proves a powerful sudorific. The dose is ½ oz., and is repeated after two or three hours. The action appears to be somewhat similar to that of the antipyretics now in vogue—antipyrin, phenacetin, etc.—drugs which, when given in combination with quinine in the routine treatment of malarial fevers, although they have no curative properties, sometimes contribute very markedly to the relief of headache and febrile distress. They must be used with great caution in adynamic cases. At the present time these drugs are much abused in many malarial countries.

Cinchona febrifuge is a preparation containing the total alkaloids extracted from cinchona bark, made in the Government factories in India and issued in the form of 3½-gr. tablets. Owing to its cheapness it is much in use in that country, and, according to Acton, it is especially useful in benign tertian infections on account of the high percentage of quinidine it contains.

Mode of action of quinine.—In what way quinine acts has not yet been satisfactorily explained. Some, reasoning from the toxic influence this drug exerts on many kinds of free amœbæ, say that it acts in malaria in the same way—that is, as a direct poison to the parasite. They support this view by pointing to the degenerative changes, as evidenced by imperfect staining reaction, exhibited by such parasites as persist in the blood after administration of quinine has been commenced. Others maintain that it acts in stimulating the phagocytes, the natural enemies of the parasite. Some experimentalists allege, on the other hand, that it paralyses the white corpuscles. That quinine does not kill all blood protozoa is certain, for it has no effect on the hæmoprotozoa of birds and reptiles, or on the trypanosomes. Certain it is that in man, with the exception of the crescent body, it usually quickly causes the

Digitized by Google

parasite to disappear from the general circulation, for the asexual forms of the benign and subtertian parasites disappear from the circulation within four days, while crescents take three weeks or more to disappear in a subject on 30 gr. of quinine a day.

Strange to say, quinine, especially in small doses, seems sometimes to wake up latent malaria and to bring about an ague fit. The same may be said of a course of mineral waters, of hydropathic treatment, and of sea-bathing.

Treatment of bilious remittent. — In bilious remittent and other severe forms of malarial fever one must not wait for the remission before giving quinine. To wait for remission or sweating used to be the practice; it was said that to give quinine at any other time was wrong, and that something terrible would happen if the superstition were ignored. *In all grave fevers a full dose, 10 or 20 gr., should be administered at once.* The parasite cannot be attacked too soon. It is desirable to have the bowels freely opened; quinine undoubtedly acts better then. It is a mistake, however, to delay the administration of the specific pending the action of the aperient. If an aperient be indicated, it should be given along with the quinine; 5 gr. of calomel is the best. Thereafter the quinine, in 5- or 10-gr. doses, should be repeated every three or six hours until fever has subsided. If there be much bilious vomiting, an emetic of ipecacuanha or repeated draughts of hot water will clear the stomach and perhaps, after a time, enable it to retain the quinine. The drug is sometimes more readily retained if given in chloroform water or in effervescing form. Mustard poultices to the epigastrium, small hypodermic injections of morphia, ice pills, sips of very hot water, effervescing mixtures, champagne, 1- to 2-drop doses of tincture of iodine, are each of them, on occasion, aids in stopping vomiting. If these measures fail, and if the vomiting is so frequent and so severe that the dose is immediately rejected, and if there is no diarrhœa, it is advisable to clear out the rectum with an injection of warm water and, when the action of this has concluded, to give an enema of 30 gr. of quinine in 3 to 10 oz. of water with a few drops of acid to aid solution; at the same time, 5 gr. of calomel may be given by the mouth. This failing, or in preference to this, recourse must be had at once to intramuscular injections. So soon as the stomach has quieted down, quinine may be given again by the mouth.

Treatment of hyperpyrexia. — Hyperpyrexia must be promptly met by prolonged immersion in the cold bath, rectal injections of iced water, ice-bags to the head, etc. At the same time

Digitized by Google

quinine must be injected intramuscularly, or into the rectum or into a vein, in full doses, and repeated every three hours until 30 or 40 gr. or more have been given. Prompt action in these cases is of the first importance, and may save life. If temperature be kept down for three or four hours the quinine gets time to act on the parasites crowding the intracranial vessels; but if temperature be allowed to mount and to remain high the patient is destroyed before the specific has a chance. The cold bath, therefore, is absolutely necessary. In such circumstances, antipyrin and similar antipyretics are worse than useless. Good rules are to prepare to give the cold bath or cold pack if the axillary temperature reaches 106° F., and to remove from the bath when rectal temperature has fallen to 102° F. Although the temperature has been reduced by this means, thermometrical observations must be continued at short intervals, say every two hours; directly it begins to rise again, say to 102°–103° F., the patient should be replaced in the bath; this must be repeated as often as necessary. Patients who have suffered from a hyperpyrexial attack should be invalided home.

Treatment of algid and hæmorrhagic forms.—As in other pernicious attacks, quinine-therapy must be vigorous. Should the intestinal hæmorrhage be urgent, it may be necessary to combine with it opium.

Other drugs in malaria.—During the continuation of a fever one has never seen much, if any, good from arsenic. The place of arsenic is not as a substitute for quinine during fever, but as a blood restorer after fever. Manson records cases of obstinate ague cured by ½-drachm doses of liquor arsenicalis; but it is not advisable to have recourse to these heroic doses. Salvarsan, novarsenobillon, and galyl may possess some parasiticidal properties, but the consensus of opinion is that they are useful rather in stimulating the blood-forming tissues in extreme anæmia and cachexia. In those cases, however, in which from some idiosyncrasy the patient is unable to take quinine, it may be necessary to have recourse to other drugs, such as methylene-blue in doses of 2 to 3 gr., and pushed until the urine becomes deeply tinged or signs of kidney irritation appear.

Treatment of splenic tumour and malarial cachexia.—The enlarged spleen of malarial cachexia is best treated by counter-irritation (linimentum iodi, or ung. hydrarg. biniodid.) and saline aperients, combined with quinine, arsenic, and iron. The subjects of hepatic enlargement and abdominal congestion arising from malarial disease of long standing generally derive

Digitized by Google

much benefit from a course of Harrogate, of Kissingen, of Carlsbad, or of other aperient mineral water. When these waters cannot be obtained, a morning aperient saline, kept up for two or three weeks, is an efficient substitute. Aperient courses should, as a rule, be combined with moderate doses of quinine, and be followed by courses of iron and arsenic. Cachectics should leave the malarial centre where they are being poisoned, and spend at least one year in Europe. They must be careful to clothe warmly, especially on first entering colder latitudes; to keep lightly employed both in body and mind; to avoid over-fatigue, constipation, exposure to a very hot sun, high winds, rain; to live temperately and, generally, to follow the dictates of common sense. Residence in a dry, cool, sunny climate, or a sea-voyage, is an admirable restorative in malarial cachexia.

Malarial cachectics must exercise great caution about exposing themselves to the fresh sea-breezes on the return voyage to Europe. Neglect of this is nearly sure to be punished with an attack of fever, sometimes of fatal blackwater fever. Many such fatalities occur yearly in cachectics from West Africa during the voyage to Europe. Return to Europe in the winter season should, if possible, be avoided, the colder months being spent in the Canaries, Egypt, or the Riviera. *If quinine is being taken when the patient leaves for Europe, its use, in the accustomed dose, should be systematically continued during the voyage and for several months (at least three) after arrival.* One finds that malarial cachectics are often allowed to start on the voyage to Europe inadequately instructed on these important points.

Treatment of malaria complicated by dysentery.—When malaria is complicated by bacillary dysentery, in addition to quinine-therapy prompt injection of antidysenteric serum combined with aperient sulphates must not be neglected. In amœbic dysentery emetine and ipecacuanha are indicated.

Food and drink in malaria.—The food in malarial fevers ought to be light and principally fluid. Effervescing mixtures often help to clean the tongue and settle the stomach. Lemon decoction (made by boiling for half an hour a sliced lemon, including skin and seeds, in a pint and a half of water, straining, diluting, and sweetening) is much relished in remittents, and may be taken systematically by all malarials with advantage. Fresh lemonade, fresh lime-juice, weak cold tea, and iced water sipped are all of them much appreciated by these patients. During convalescence the quality of the food should be gradually improved and, if necessary, supplemented by a light wine or bitter ale.

Digitized by Google

Prophylaxis

The basis of malaria prophylaxis is the fact that particular species of mosquitoes are indispensable for the propagation of the parasites. Practical measures, therefore, have for their object the extermination of these insects, or, failing this, the prevention of their bites. War need not be waged against all mosquitoes; our present knowledge seems to indicate that only the Anophelinæ have to be considered. As the members of this sub-family are easily recognized (p. 92), and ast hey are somewhat fastidious in their habits, their extermination in limited areas is by no means a hopeless task. Complete extermination of mosquitoes, or even of all anophelines, by antilarval measures has been found to be impossible. It is much more practical to concentrate on particular species which are known to be efficient carriers of the disease. Since many kinds have a particular habitat, special measures are necessary in special circumstances. James lays stress upon the beneficial results to be obtained by destruction of the adult insects in dwelling-houses, and the necessity for further research upon the range of flight of the anophelines, since this has been found to be much greater than was formerly thought to be the case.

Drainage, cultivation, and flooding.—Experience has shown that much can be done to free a locality of malaria. Drainage and cultivation where the land will repay the expenditure, permanent and complete flooding where it will not and where such flooding is possible, proper paving and draining of unhealthy towns, and the filling-in of stagnant, swampy pools—these are the more important things to be striven for in attempting the permanent sanitation of malarious districts. In England, in Holland, in France, in Algeria, in America, and in many other places, enormous tracts of country which formerly were useless and pestilential have been rendered healthy and productive by such means.

In carrying out extensive public works care should be exercised to provide good subsoil drainage in connection with irrigation, to provide efficient drainage to carry off superfluous water *before* introducing a larger water supply into a town previously inadequately watered, and to avoid interfering with the natural drainage of a district in constructing railways and so forth. To do anything that may raise the level of the subsoil water in potentially malarial districts is most dangerous. Equally so is the neglect to fill up or provide for the drainage of excavations, such as the " borrow-pits " in railway construction or similar holes in which rain-water may accumulate and create breeding pools for mosquitoes.

Digitized by Google

Location of dwelling-houses.—The inhabitants of malarious districts ought to live in villages or towns with well-paved streets and courts, going out to cultivate their fields during the day, but returning to sleep in the town before nightfall. Houses should be placed, if possible, on high and dry situations, a clay soil being avoided. All forest undergrowth should be cleared away. It is unwise in countries such as Africa, where nearly all Europeans suffer from chronic malarial poisoning, to place dwelling-houses in exposed situations, or where high winds are apt to produce chills and consequent fever relapses. For the same reason, in elevated situations houses should be well sheltered by trees planted at some distance from the premises, or by higher ground. In the neighbourhood of houses the felting of natural grass should, if possible, be preserved, or, if it be disturbed, replaced immediately, or the exposed soil covered with rammed clay or cement. It is unwise to have flower-beds or vegetable gardens near bedroom windows, or to allow water from bathrooms or cookhouses to flow over the ground in the vicinity of the house, or to keep water unchanged in tubs or waterbutts for mosquitoes to breed in. Pools and puddles of stagnant water should be filled up and turfed. Waterbutts and cisterns should be screened, and sagging roof-gutters rectified; discarded tins, jars, pots, bottles, and all rubbish capable of holding water in which mosquitoes could breed should be got rid of, and plants or trees in which collections of water occur should be cut down. Ponds should be stocked with fish, as fish tend to keep down mosquitoes by preying on their larvæ. The neighbourhood of swamps is to be avoided. A few ounces of petroleum thrown on the surface of a pond will prevent mosquitoes from depositing their eggs on the water, and will asphyxiate their larvæ; the petroleum requires to be renewed from time to time—say once a week. Coal tar may be used in the same way. Roubaud has recently shown that powdered formalin is most destructive to anopheline larvæ, while at the same time harmless to other forms of life, such as fish. It is sprinkled in quantities from 25 to 35 cg. (3·8 to 5·4 gr.) to one square metre of water. The granules are ingested by the larvæ, which thereby become poisoned. Water treated in this manner can be used for cattle, irrigation, and laundry work. There are many other simple precautions which will occur to every prudent man, and which, in malarious countries, he should take care to have carried out.

Danger from the vicinity of natives.—Seeing that in malarious localities a large proportion of the native children harbour the malaria parasite, and that a large proportion of the anophelines

Digitized by Google

in the neighbourhood of native houses are infected, it is manifest that to visit native quarters when mosquitoes are feeding, especially in the evening or during the night, is fraught with danger. For the same reason the European should build his house or pitch his camp well away—a quarter of a mile at least—from native quarters, and beyond the flight of infected anophelines; and, for the same reason, native children should not be allowed to frequent European establishments.

Cultivation of trees and plants.—Much was expected at one time from the cultivation of eucalypti of different species—particularly *Eucalyptus globulus*—as a means of suppressing malaria. Specific virtues were attributed to its balsamic exhalations. These hopes have not been fulfilled in every case; but, undoubtedly, the effect of this rapidly growing tree in drying the soil is of use in some localities. The same may be said of the cultivation of the sunflower, chrysanthemum, kiri tree, and other plants. Possibly these plants influence insect life in other ways.

Native experience to be consulted.—It is unwise to build where the natives say the neighbourhood is unhealthy; natives generally know such places. Neither, if it can be avoided, should a stay be made where the natives are anæmic and have enlarged spleens—sure indications of an unhealthy district.

Other precautions. — Bedrooms should be situated in an upper storey, and dwelling-rooms be well raised on piles or arches above the ground. Common sense tells us that campaigns and journeys in malarious districts should be conducted and concluded during the healthy season, if there be one. *Mosquito-nets must invariably be used;* many travellers attest their value, so plainly indicated by recent discoveries. The body should be covered up during sleep, and every precaution (as fires, etc.) that circumstances permit should be employed to keep mosquitoes away.

The subjects of malarial infection are dangerous to their companions; they should, therefore, be avoided or, if this is impracticable, compelled to sleep under efficient mosquito-nets. Mosquitoes must be rigorously excluded from hospitals. It will prove a truly economical procedure to supply natives liberally with quinine; this should go hand in hand with other steps that may be taken to render a place salubrious.

Mosquito-veils.—Fig. 22 shows a practical method of protecting the head and neck from mosquitoes while on night duty; these veils, the invention of Mrs. W. J. Simpson, can be procured under the name of "Simpsonette."

Digitized by Google

Mosquito-protected houses.—It has been proved experimentally and practically that complete protection from mosquito bite, and therefore from malaria, can be secured by having the dwelling-house protected by gauze fittings, with a mesh not larger than twelve strands to the inch, in the doors, windows, chimneys, and ventilators. When possible, such measures should be adopted and intelligently applied. Some such arrangement will, in the near future, be a feature in the domestic architecture of malarial countries.

Fig. 22.—Mosquito-veil to protect head and neck.
("*Trans. Soc. Trop. Med. and Hyg.*")

Quinine and arsenic as prophylactics.—As regards the use of quinine as a prophylactic, opinions are divided. The experience of the War has been, on the whole, to underrate rather than overrate its prophylactic value. The practical outcome is that quinine prophylaxis is inapplicable to scattered bodies of men under inadequate medical supervision. In highly malarious localities it is advisable to give 15 gr. every other day, in liquid form, towards evening, on a full stomach; in more salubrious localities it may be given in 6-gr. doses every night. The hydrochloride in gluten-covered tablets may be administered in pill form; at any rate, when dealing it out to soldiers it is important

Digitized by Google

to see that the drug is swallowed. Apparently it is by no means so efficacious in preventing subtertian as in preventing benign malaria. Probably the different opinions as to the value of prophylactic quinine depend upon the strain of malaria parasite concerned. Some are more sensitive than others to quinine. Most deny that arsenic possesses any prophylactic power whatever.

Other prophylactics.—Tea, coffee, and very small doses of alcohol are also decidedly of service; but they should be used in strict moderation, the last being taken only after the work of the day is over, and when there is no longer any necessity for going out in the sun. Crudeli speaks highly of lemon decoction (made as already described, p. 77) as a prophylactic; its use can do no harm, and it is a pleasant, slightly tonic, and slightly aperient beverage, well suited as a drink in hot climates. The decoction made from one lemon may be taken daily in divided doses.

Education.—It is impossible to lay down directions for the prevention or suppression of malaria which would be applicable at all times and to all places, and in every circumstance. What might suit one set of conditions might not be appropriate under other conditions. But by one, or other, or all of the measures indicated above, much can be done to mitigate or avoid endemic malaria. Perhaps the most important initial measure in the struggle with the pestilence is the education of the inhabitants of malarial countries in the mosquito-malaria theory. Sanitary measures can rarely be carried out effectually without the co-operation of those whom they are intended to benefit; and this cannot be secured unless the rationale of their operation is understood. Therefore, those responsible for the public health in malarial districts should, by one means or another, indoctrinate the people in the mosquito-malaria theory. If he succeed in this, the sanitarian will have an easier and a more hopeful task.

Digitized by Google

CHAPTER V

MALARIA AND THE MOSQUITO

THE part played by the female mosquito, or gnat, in the life-history of the germ of malaria, as well as in that of yellow fever, of filariasis, of dengue, and perhaps of other diseases of warm climates, renders some knowledge of the natural history of this insect a necessity for the tropical pathologist.

Although the Culicidæ or mosquitoes had received, now and again, some attention from naturalists ever since the time of Linnæus, it is but recently that the extent, complexity, and importance of this group of insects have been apprehended. Considerations of space preclude more than the merest outline of the subject; those who desire to follow it up would do well to provide themselves with one, or more, of six recent works—namely, "The Mosquitoes of North and Central America and the West Indies," by Howard, Dyar, and Knab; Alcock's "Entomology for Medical Officers," Patton and Cragg's "Textbook of Medical Entomology," Blanchard's "Les Moustiques," Giles's "Handbook of the Gnats or Mosquitoes," and "Malaria at Home and Abroad," by James —in which will be found details of all that was known about these insects up to the date of their publication.

The **Culicidæ**, of which there are at least 500 known and, probably, over 200 additional and as yet undescribed species, belong to the order of Diptera, or two-winged insects, in which the posterior of the two pairs of wings of the typical insect are rudimentary, being represented by the *halteres* or balancers (Plate VII. and Fig. 23). Like most other members of the order, they lay *eggs*, from which are hatched worm-like *larvæ*; these, after growth and several changes of skin, cease to eat, and become converted into *nymphs* or *pupæ*, from which, by a rupture of the pupa-case, the adult insects or *imagines* emerge.

The geographical range of the mosquito extends from the frigid zones to the equator. Given stagnant or slow-flowing water and a summer temperature, this family of insects will be represented by one or many species. The distribution of particular species and the abundance of mosquitoes in any given place are determined, in addition to temperature and hydro-

Digitized by Google

meteorological conditions, by complicated circumstances not yet wholly understood.

The adult insect feeds on vegetable juices; the males, with few

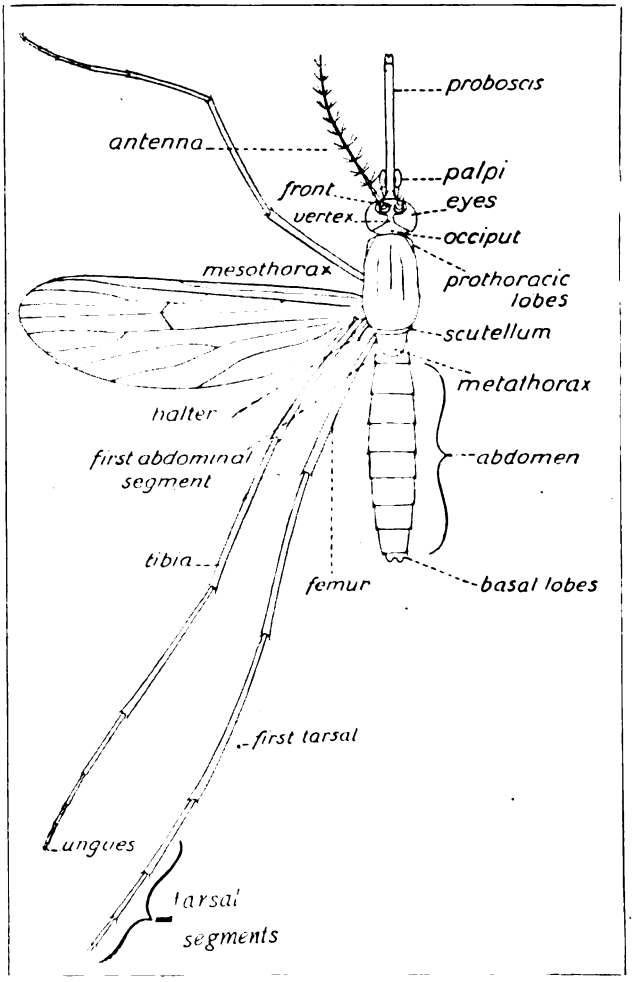


Fig. 23.—Female mosquito.

exceptions, exclusively so. In addition to a vegetable diet, the females of most species, when opportunity offers, suck the blood of mammals, birds, occasionally of fishes, reptiles, and even that

Digitized by Google

of other insects and their larvæ. The male mosquito, not being a blood-sucker, takes no part in the diffusion of disease; it is the female only that is a germ carrier. (Fig. 23.)

Soon after impregnation the female lays her eggs (Figs. 24, 25, 26) from time to time—singly, in groups, or in boat-shaped masses, according to species—either on the surface of still water, on which

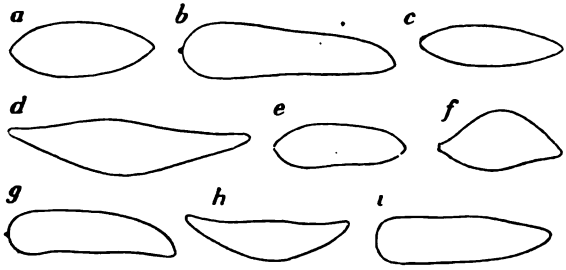


Fig. 24.—Various forms of mosquito eggs.

a, Grabhamia dorsalis; *b*, Culex pipiens; *c*, Culex scapularis; *d*, Mansonia titillans; *e*, Stegomyia calopus (fasciata); *f*, Tæniorhynchus fulvus; *g*, Culex fatigans; *h*, Jauthinosoma mexicanum; *i*, Tæniorhynchus fasciolatus.

they float, or in propinquity to water. The process of hatching out depends in great measure, as indeed do all the developmental processes connected with the mosquito, on temperature, being retarded or even suspended by cold and accelerated by warmth.

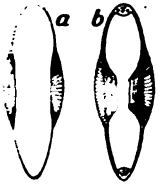


Fig. 25.—Eggs of Anopheles maculipennis.

a, Under side; *b*, upper side.

Fig. 26.—Culex fatigans—egg-boat. (*After Sambon.*)

In some species the eggs remain dormant throughout the winter or through a long spell of dry weather, but in ordinary circumstances the larvæ hatch out in from two to three days, and at once proceed to feed voraciously on the organic material suspended in the water. Being air-breathers, a great part of their time is passed at the surface of the water, where they lie in such a position—which varies with species—that the respiratory opening, placed near the tail, can function readily (Figs. 27, 28). After the several moultings the

Digitized by Google

larva, now very much increased in size, passes to the nymph or pupa phase (Figs. 29, 30), during which the little animal ceases to feed, and for the most part floats just awash at the surface of the water. In from one to two days the pupa-case bursts and the insect, emerging, stands on the empty case till its wings have dried, when it flies away. From first to last, from egg to imago, the

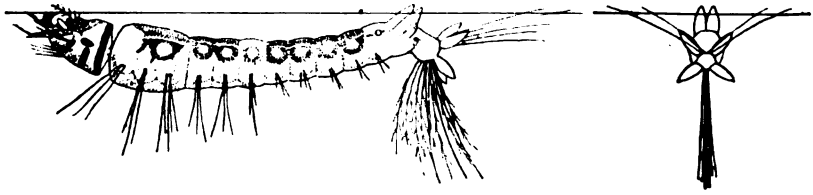


Fig. 27.—Anopheles maculipennis, Meig., larva, showing breathing position at surface of water. (*After Howard, "Bull. United States Dept. Agr."*)

process of development takes about a month in the temperature of the Italian summer; but a much shorter time (seven to ten days) may suffice in a tropical climate. As each female mosquito may lay eggs many times in a season, and many hundreds of eggs each

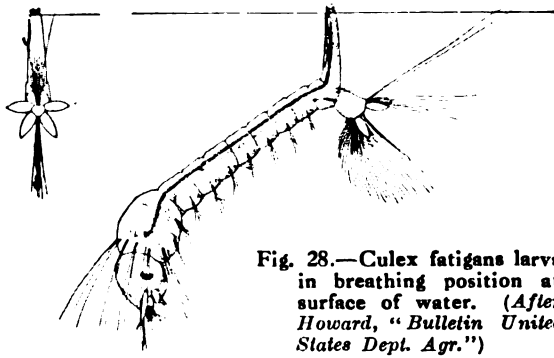


Fig. 28.—Culex fatigans larva in breathing position at surface of water. (*After Howard, "Bulletin United States Dept. Agr."*)

time, and as the young female can produce eggs within a week or ten days after her emergence from the pupa-case, it follows that one pair of insects can give rise to a large progeny in the course of a summer.

During cold weather the development of the larva is temporarily suspended, and the surviving adults, at all events the females, hibernate in dark and sheltered places, to become active again on the return of warm weather. In this way the species is carried

Digitized by Google

over the cold weather of winter, though there are some species that hibernate in the larval stage and others in the egg. The duration of the life of the adult insect has not been definitely ascertained; it is known that some species, if supplied with water and suitable food, can live for several months.

It is suggested that the mosquito tends to return to the particular pool in which she herself was hatched out to deposit her own eggs, and that she rarely strays from the vicinity more than a few yards, quite exceptionally beyond half a mile. Occasionally she may be blown for some distance by gentle winds; and it is believed that in certain circumstances, probably connected with food supply and over-stocking, she will travel singly or in vast swarms for

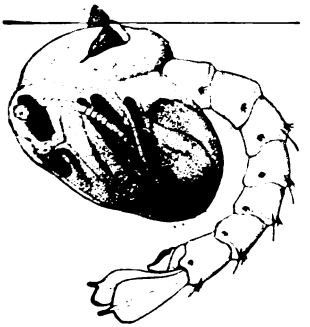


Fig. 29.
Pupa of Anopheles maculipennis.

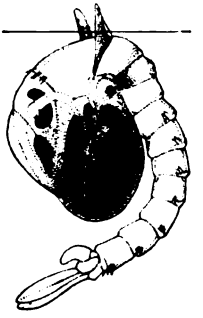


Fig. 30.
Pupa of Culex fatigans.

long distances. Such migrations, however, are quite unusual. Of course, mosquitoes may be, and often are, transported great distances in ships, railway carriages, and similar vehicles, and in this way man aids in their diffusion; but for the most part the mosquito is a feeble and timid flyer, disliking to leave her accustomed haunt, and seldom rising high above the ground. So soon as even a moderate breeze springs up she seeks shelter in bush, or house, or cranny. Some species are domestic; others live exclusively in jungle or forest; some, after passing the day in the open, visit human habitations, or the haunts of birds and beasts, during the night. The great majority of species are nocturnal in habit, although many of these can be coaxed into activity by the reproduction of night-like conditions of shade and atmospheric stillness.

Figs. 23–35 give a good idea of the leading features of the anatomy of the mosquito and of the names applied to the various parts and organs, and will help the student to understand

Digitized by Google

descriptions of genera and species. For the generic distinctions based on scale characters, *see* Figs. 36–38.

The antennæ of the male insect (Figs. 31, *a*, and 32, *a*) are usually adorned with a profusion of long, silky hairs, in marked contrast to the scanty, down-like, and short hairs on the antennæ of the female; this is an easily recognized indication of sex in most species.

The proboscis consists of a number of piercing elements enclosed in a sheath—the labium, which, at its free end, is tipped with two minute labella. In feeding, the mosquito raises her hind legs and presses the tip of the proboscis against the skin. This causes the

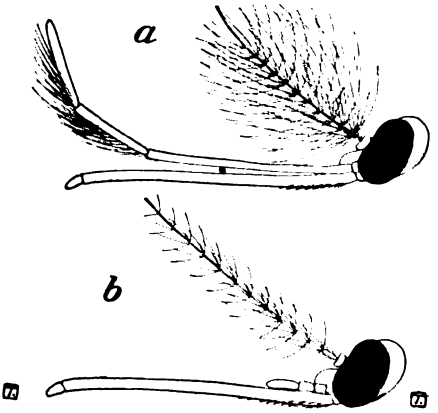


Fig. 31.—Heads of Culicini.
a, Male; *b*, female.

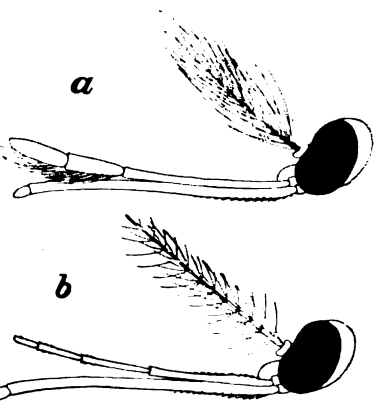


Fig. 32.—Heads of Anophelini.
a, Male; *b*, female.

labella (Fig. 33, *h*) to splay out and so serve as a support to the piercing elements—namely, the labrum, hypopharynx, mandibles, and maxillæ (Figs. 33, 34)—which are now thrust into the skin. The labium does not penetrate; as the stabbing elements sink into the skin it bends backwards about its middle, the labella still pressing against the skin and clasping the stilettes. The secretion of the salivary glands (Figs. 10, 16) passes along the salivary duct and thence down a minute canal which traverses the hypopharynx to its tip, and so into the subcutaneous tissues of the bitten animal. It is supposed that the function of this secretion is, by irritating, to determine a flow of blood to the part bitten, and also to prevent coagulation of the blood. To many people this secretion is a powerful irritant, although repeated inoculation tends to produce tolerance, as in the case of many other organic poisons.

Digitized by Google

A buccal tube is formed by the apposition of the upper surface of the hypopharynx to the under surface of the labrum (Fig. 34). Along the tube so formed the blood is aspirated by the expansion of the gizzard-like organ (Fig. 10, *b*), and then driven by the contraction of the same into the stomach (Fig. 10), or middle intestine, as it is called. A mosquito will fill herself in a minute or thereabouts. She then withdraws her proboscis and flies heavily away to some sheltered spot to digest the meal. Apparently the first step in digestion is the concentration of the blood she has imbibed; this is effected by excretion of the watery portion of the liquor sanguinis. Often while this process of dehydration is proceeding, even while she is sucking, droplets of clear fluid may be seen ejected

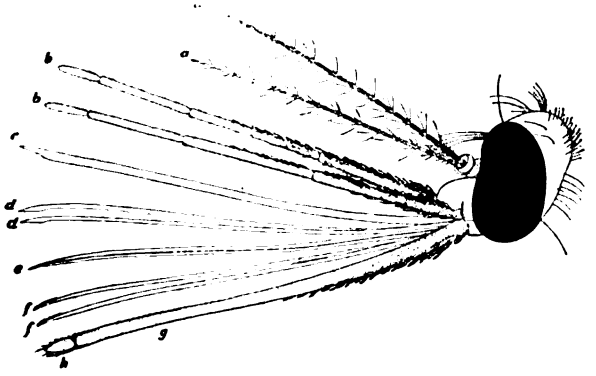


Fig. 33.—Mouth-parts of female mosquito.
a, *a*, Antennæ; *b*, *b*, palpi; *c*, labrum-epipharynx; *d*, *d*, mandibles; *e*, hypopharynx; *f*, *f*, maxillæ; *g*, labium; *h*, labella.

at her anus. The concentrated blood becomes in this way a viscid tarry mass, which is gradually, in the course of three or four days, partly absorbed, and partly voided as gamboge-coloured fæces. The mosquito is now ready for another meal.

The rich pabulum supplied by blood seems to favour ovulation.

Diagnosis. — Many kinds of insects possess blood-sucking propensities. As a rule there is little difficulty in distinguishing most of these from the mosquito. There are certain Diptera, however, which closely resemble the latter in their appearance as well as in their habit. These the student should learn to distinguish.

The principal of the mosquito-like blood-suckers are the Midges (Chironomidæ) and the Sandflies (Phlebotomus). The following are the diagnostic points:—

Digitized by Google

Mosquitoes have a long suctorial proboscis, and the veins of their wings are fringed with scales.

Midges are very slender and minute, have a short suctorial apparatus, and their wings are devoid of scales.

Sandflies are small, slender, and very shaggy, have a comparatively short suctorial apparatus, comparatively long legs; narrow, pointed, hairy wings, and long hairy antennæ.

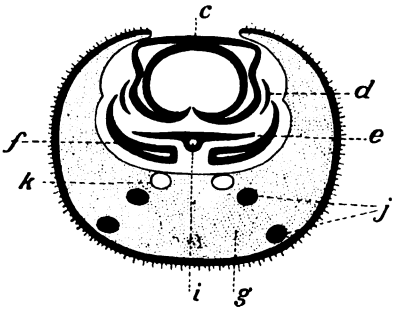


Fig. 34.—Section of mosquito's proboscis.
(Adapted from Nuttall and Shipley.)

c, Labrum-epipharynx; d, mandible; e, hypopharynx; f, maxillæ; g, labium; i, salivary duct; j, muscles; k, trachea.

The medical man should be able not only to recognize mosquitoes but also to determine genera and species. Obviously, it would be impossible to give here minute descriptions of the large number of species that have been described; the reader is therefore referred to the monographs on the subject already mentioned. On the next page is given a **synoptical table** which will enable the student to identify the main groups or sub-families to which any given mosquito belongs. It has been prepared after a careful consideration of the various classifications proposed. Most authorities separate

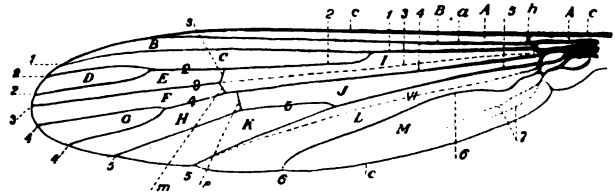


Fig. 35.—Wing of Culex concolor (male), to illustrate terminology.

c, Costa; a, auxiliary vein; 1–6, first to sixth longitudinal veins and branches; 7, seventh or false (unscaled) longitudinal vein; VI., unscaled vein between fifth and sixth longitudinal veins; h, humeral transverse vein; s, supernumerary transverse vein; m, middle transverse vein; p, posterior transverse vein; A, costal cells; B, subcostal cells; C, marginal cell; D, anterior fork cell or first submarginal cell; E, second submarginal cell; F, first posterior cell; G, hinder fork or second posterior cell; I, first basal cell; J, second basal cell; K, anal cell; L, axillary cell; M, spurious cell.

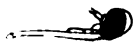
the Culicidæ into two sub-families, namely—(1) Corethrinæ, in which the proboscis is short and not formed for piercing; (2) Culicinæ, or typical mosquitoes with elongate proboscis. The Culicinæ again are arranged in four natural tribes according to the table.

Digitized by Google

SUB-FAMILY CULICINÆ: TABLE OF TRIBES

Proboscis

Straight.



A

Nude.

C

Scutellum

Trilobate: abdomen completely invested with close overlapping scales ... ... *Culicini.*

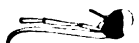
Simple, not trilobate: abdomen never completely and uniformly covered with scales ... ... *Anophelini.*

D

E

With a tuft of bristles: a pair of very large bristles projecting horizontally forward from crown of head ... ... *Sabethini.*

Tapering and recurved.



B

Flat scales on all parts of body: large, iridescent mosquitoes ... ... *Mcgarhini.*

The *Megarhini* are jungle mosquitoes. From the structure of their proboscis it is very improbable that they can bite. Their larvæ, which occur chiefly in the water that collects in holes in trees, bamboo-stumps, etc., are predaceous, and undoubtedly destroy the larvæ of other mosquitoes having the same breeding habits. The *Sabethini* are also jungle mosquitoes, breeding almost exclusively in the water that collects in the axils and bracts of leaves and in "pitchers" and other such modified parts of plants.

Digitized by Google

GENUS ANOPHELES (Meigen). (Plate VII.)

Head only moderately broad, usually covered with upstanding **forked scales**, though scales of other kinds are also present in a few

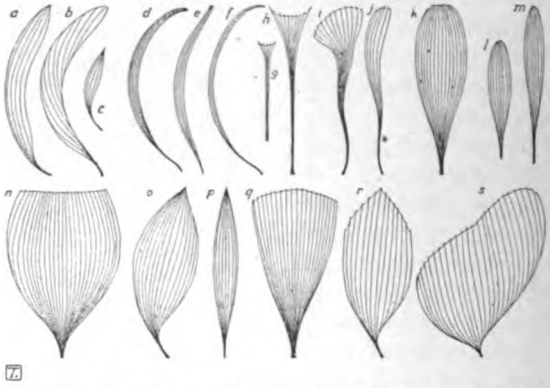


Fig. 36.—Graphic key to generic distinctions based on scale characters.

b, *c*, Narrow curved scales; *d*, *e*, *f*, hair-like curved scales; *g*, *h*, upright forked scales: *i*, *j*, long twisted scales; *k*; large lanceolate scale; *l*, *m*, small narrow lanceolate scales; *n*, large expanded scale; *o*, *p*, spindle-shaped scales; *q*, broad flat scale; *r*, *s*, broad irregular scales.

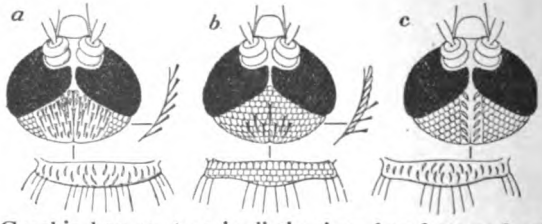


Fig. 37.—Graphic key to generic distinctions based on scale characters.

a, Anopheles, head, scutellum, and lateral view of head scales; *b*, Stegomyia, head, scutellum, and lateral view of head scales; *c*, Ædes, head and scutellum scales.

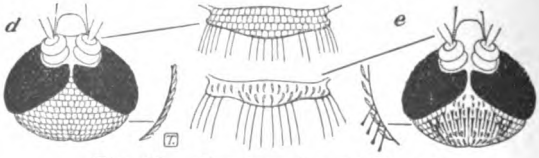
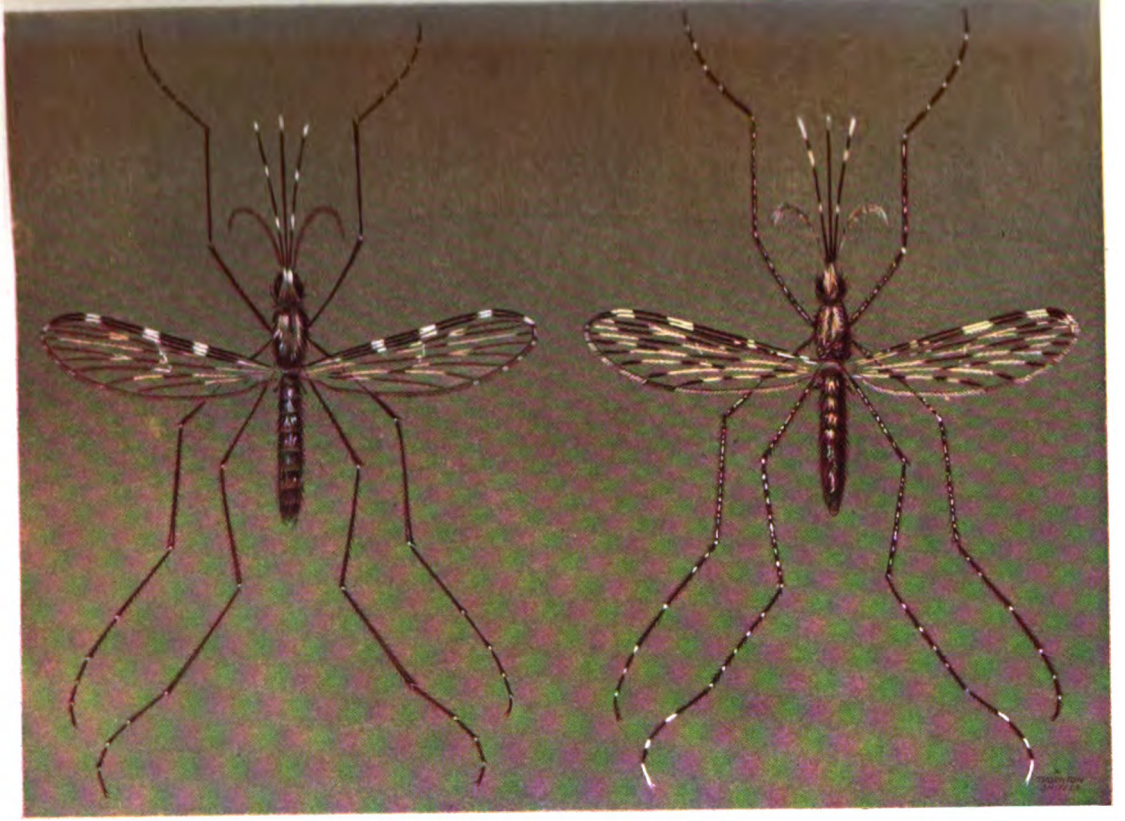


Fig. 38.—Continuation of Fig. 37.

d, Megarhinus, head, scutellum, and lateral view of head scales; *e*, Culex, head, scutellum, and lateral view of head scales.

species. (Figs. 36–38.) Maxillary palps long and spathulate in the male; as long as, or not much shorter than, the proboscis in the female. Free edge of scutellum simply convex, not trilobate;

Digitized by Google



Anopheles funestus, Giles.
India.

Anopheles maculatus, Theobald.
Malaya.

TWO MALARIA-CARRYING ANOPHELES. × 14.

PLATE VII

Digitized by Google

Digitized by Google

metanotum bare. Abdomen either sparsely hairy or with localized patches of scales; sometimes with a considerable expanse of scales which, however, never form a uniform, complete, and compact investment. Wings commonly dappled or profusely speckled, but occasionally quite spotless. Legs remarkably elongate. In repose the body is usually inclined at an angle with the resting surface. (Figs. 41, 42.)

The eggs are boat-shaped, and with rare exceptions have their investing membrane inflated laterally to form a pair of floats.

The larva has the head at least as long as broad, and has four bristles or feathered hairs projecting from the free edge of the clypeus. The long lateral hairs of the thorax and abdomen are

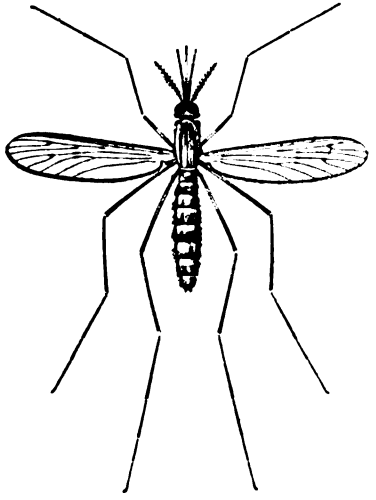


Fig. 39.—Anopheles maculipennis (female).

strongly feathered. Some or all of the abdominal segments as far as the 7th carry dorso-laterally a pair of characteristic rosettes or cockades of scales. The breathing openings are situated in a hollow on the dorsum of the 8th segment, the hollow being bounded laterally and posteriorly by a system of folds or valves.

The larvæ occur not only in all kinds of stagnant water, but also in pools in the beds of rivers and mountain streams, or even in the current if there is also floating weed and débris for their protection, in domestic water-vessels, and occasionally in the water that collects in holes in trees; some species thrive in brackish, or salt water, and each species has its own particular kind of habitat.

Digitized by Google

For those who still think it desirable to subdivide the genus *Anopheles*, the following synopsis of subgenera may be serviceable :—

SYNOPSIS OF SUBGENERA OF ANOPHELINI

Front edge of wing either not spotted or having not more than two distinct spots.

- Abdomen without scales; palpi slender; wings not or little spotted; wing-scales narrow ... ... "*Anopheles.*"
- Abdomen with some localized scales, if only a tuft on the 7th abdominal sternum; palpi shaggy; wings always dappled; wing-scales broad ... ... "*Myzorhynchus.*"

Front edge of wing broken into *numerous* alternate light and dark spots or streaks.

- Mesothorax invested with hairs ... ... "*Myzomyia.*"
- Mesothorax invested with narrow upstanding scales ... ... "*Pyretophorus.*"
- Mesothorax invested with broad, appressed, white or yellow scales
  - No outstanding tufts of scales on abdomen ... ... "*Nyssorhynchus.*"
  - Tufts of scales projecting from abdomen laterally or ventrally ... "*Cellia.*"

SPECIES THAT ARE KNOWN TO FOSTER THE MALARIA PARASITES

NOTE.—In the case of several species it is known that they are not always susceptible to experimental infection throughout their

Digitized by Google

intergeographical range, and that at a given time and place all individuals are not in an equal state of susceptibility.

Fig. 40.—Resting position of Culex pipiens.

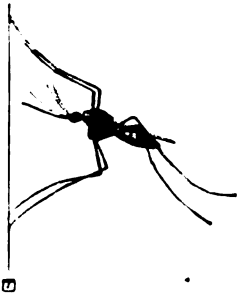


Fig. 41.—Resting position of Anopheles sinensis.

Fig. 42.—Resting position of Anopheles maculipennis.

EUROPE.—*A. maculipennis*, *A. sinensis* (= *pseudopictus*, Grassi), *A. superpictus*, Grassi (= *palestinensis*, Theob.), *A. hispaniola*, Theob. (= prob. *turkhudi*), *A. bifurcatus*, *A. plumbeus*.

AFRICA.—*A. maculipennis*, *A. umbrosus* (= *strachani*), *A. mauritianus*, *A. culicifacies* (= *Pyretophorus sergenti*, Theob.), *A. funestus*, *A. turkhudi*, *A. costalis*, *A. maculipalpis*, *A. pharoensis*.

ASIA.—*A. umbrosus*, *A. barbirostris*, *A. sinensis* (= *jesoënsis*), *A. culicifacies*, *A. palestinensis* (= *superpictus*, Grassi), *A. funestus* var. *listoni* (= *formosaënsis* and *umbrosus*), *A. minimus*, *A. turkhudi* (= *A. hispaniola*), *A. ludlowi*,* *A. umbrosus*, *A. leucosphyrus*, *A. stephensi*, *A. fuliginosus*, *A. maculatus*, *A. maculipalpis*, *A. theobaldi*, *A. willmori*, *A. pulcherrimus*, *A. albirostris*, *A. bifurcatus*, *A. pharoensis*.

NORTH AMERICA.—*A. crucians*, *A. punctipennis*, *A. pseudopunctipennis*, *A. quadrimaculatus*, *A. albimanus*, *A. argyrotarsis*.

SOUTH AMERICA.—*A. punctipennis*, *A. pseudopunctipennis*, *A. pseudomaculipes*, *A. intermedius*, *A. tarsimaculatus*, *A. albimanus*, *A. argyrotarsis*.

CENTRAL AMERICA.—*A. lutzi*.

AUSTRALIA.—*A. bancrofti* (?), *A. annulipes* (?), *A. tesselatus* (New Guinea).

* This species has been shown by Christophers to be the transmitter of a peculiarly localized malaria in the Andaman Islands. It breeds only in brackish water, and is not found farther away from such water than half a mile.

Digitized by Google

CHAPTER VI

BLACKWATER FEVER

Synonyms. — Hæmoglobinuric Fever; Melanuric Fever; Hæmaturic Fever.

Definition.—An acute disease characterized by pyrexia—generally ushered in by severe rigor, bilious vomiting, icterus, hæmoglobinuria and, frequently, diminution or suppression of urine.

For a long time this disease, like kala-azar and several other tropical fevers, had been regarded as a form of malaria, and in earlier editions of this manual, in deference to general opinion, it was placed, with some reservation, in the same section as that disease, but, considering that the etiology is still in doubt, it was afterwards thought advisable to allot to it a separate chapter.

Geographical distribution.—The geographical distribution of blackwater fever is very wide. Although the endemicity of blackwater fever is not coextensive with that of malaria, it is only in localities in which malaria of the subtertian type is very prevalent that blackwater fever can be acquired. Endemic concurrence, however, must not be looked on as conclusive of identity; the germ causes of very different diseases may have certain topographical requirements in common.

The prevalence of blackwater fever in various malarious countries is most unequal. It is common here and there throughout tropical Africa. It is found all along the West Coast from the Senegal to the Quanza, but principally on the Congo and on the deltas of the Niger and Gambia rivers. On the East Coast it is also widely spread, especially along the Zambesi, the lower Shiré, and the shores of the Nyasa. It is far from uncommon in the Upper Niger, in British and German East Africa, in Uganda, in North and South Rhodesia, in Abyssinia, and in the valley of the Upper Nile and Algeria. It is also common in some parts of Madagascar.

In America it extends over the southern States of the Union, chiefly Florida, Georgia, Alabama, Mississippi, Arkansas, and Texas, but recently it has also been prevalent in North Carolina and Virginia. It is found, too, in Central America, on the Upper Amazon, on the plains of Venezuela, and in the West Indies.

Digitized by Google

In Europe it is restricted to Bulgaria, Macedonia, Albania, Greece, Sicily, and Sardinia. A few cases may have been reported from Central Italy. It is extremely rare in the Roman Campagna, the classic land of malaria.

In Asia it is reported from Palestine, especially the Jordan valley, Tonquin, the Malay Peninsula, Formosa, and lately it has been described as occurring in Assam, Burma, Darjeeling, the Terai, Meerut, and Amritsar. It occurs in many of the malarious islands—Java, Solomon Islands, etc.—of the Eastern Archipelago, and also in New Guinea.

Blackwater fever appeared among British troops in Salonica, Palestine, and East Africa during the War; in fact, whenever they were exposed to a virulent malarial infection.

Before 1885, strange to say, no Indian writer had mentioned hæmoglobinuria as a feature in the pyretology of Hindustan or of the East. Apart from the possibility of its having been overlooked, there may be another explanation for this singular silence: the disease may have been confounded with bilious remittent. It is difficult to believe, however, that the large number of acute observers, who had studied Indian diseases so carefully and for so many years, could have systematically ignored this striking disease. Possibly, therefore it is of recent introduction into India. Such an idea is countenanced by the fact that certain medical men practising in Africa, good observers, declare that blackwater fever is of comparatively recent introduction there; and, moreover, that it is yearly becoming more common in that continent. In certain States of the American Union it seems to have been only recently introduced; Meek says it first appeared in Texas in 1886.

Topographical distribution.—Although blackwater fever has a wide general distribution, it is limited in its endemicity to low, swampy grounds; and although, as reported by several authors, it sometimes occurs at high altitudes, this does not prove that infection took place there. We know that the disease may remain latent for a considerable time, that those who have been infected may have relapses at long intervals, and that the clinical manifestations may appear for the first time far from the place in which the infection was contracted. It is a common belief among the older residents in Nyasaland that a change of district, particularly from one level to another, causes blackwater fever—an opinion based on the experience that many cases occur soon after such a change. Amongst Europeans in British Central Africa such changes of district are frequent, and, as it is only a day's journey from the lowlands to the highlands, it is reasonable to infer that the majority

Digitized by Google

of the cases which occur on the highlands depend on infection contracted previously in the swampy regions at the foot of mountains and in the season during which the conditions favouring infection are most prevalent.

Seasonal prevalence.—Blackwater fever is reported to be especially frequent in late summer and in autumn in the southern States of the American Union. On the West Coast of Africa it seems to be most prevalent at the close of the rainy season (August and September). For British Central Africa we have no definite information on this point. Like other infective diseases, the acquisition of the germ cause of blackwater fever is directly or indirectly dependent on special meteorological conditions, although the first clinical manifestations of the infection and relapses may occur at any season and in any place.

Epidemiology.—Blackwater fever at times assumes an epidemic form. It may not be seen for years in a district, and then numbers of cases may occur within a short time. Very often, as is the case in yellow fever, the magnitude of an "epidemic" may depend on the number of susceptible persons, possibly new arrivals, within the endemic region. It broke out amongst the labourers employed in making the canal through the Isthmus of Corinth; it attacked the Chinese labourers on the Congo railway; and in 1885, according to Dr. Wenyon, of Fatshan, China, "it ravaged like a plague the Chinese army on the Tonquin border of Kwangsi." In collective dwellings, such as barracks, hospitals, schools, it may attack several persons at the same time. In 1885 it broke out in a prison in Castiades, Sardinia, attacking 24 out of 800 convicts. Sometimes several cases may occur at intervals in the same house; such houses are known in British Central Africa as "blackwater fever houses." In the German East African force under von Lettow it is recorded that over 60 per cent. of the medical casualties were due to blackwater fever.

The occurrence of several cases in the same family may not be one of pure coincidence, but probably may be explained by exposure to some common factor. Manson once saw a lady suffering from blackwater fever who had, with her husband and child, but lately returned to England from the Upper Zambesi. She died. Being struck by the anæmic appearance of the husband, Manson examined his blood and found he had a subtertian malaria infection; a few days later, he, too, developed blackwater fever, but recovered; the child escaped.

Predisposing causes.—Individuals of all ages and both sexes are liable to blackwater fever, but they are not equally

Digitized by Google

subject to it. It more commonly affects men about the middle period of life, obviously on account of their greater exposure either to its causative agent or to circumstances provocative of an attack.

At one time race was considered an important factor. In Africa, Europeans, Indians, and Chinese are attacked in great numbers, whilst the natives are said to enjoy an immunity. The immunity of the natives is probably not a racial immunity; more likely it is the immunity conferred by infection during childhood. In fact, negroes living in places which are free from blackwater fever contract the disease just like Europeans when they come within its reach. Plehn mentions a serious outbreak of blackwater fever among the blacks in the Cameroons, the disease especially attacking those who had come to the coast from the interior. Reynolds says that the disease occurs sporadically amongst the natives of Ashanti.

Among the circumstances which predispose to the active clinical manifestation of the blackwater-fever infection, debility from previous illness, bad food, and hardship have undoubtedly a powerful influence. It is usually in those who have suffered from subtertian infection, more rarely from tertian and quartan infections, or from dysentery, or who are "run down" from any cause, that blackwater fever appears, although cases of the disease in strong, healthy individuals of recent arrival have frequently occurred.

Length of residence.—It has been repeated again and again that Europeans are rarely attacked within the first year of residence in a blackwater-fever country, and great stress has been laid on this statement by those who believe that the hæmoglobinuria is not the special feature of a specific disease, but only a symptom of ordinary malaria in people who have previously suffered from several attacks of the prevailing intermittent fever. We know, however, that although, in most cases, attacks of the more widely spread subtertian may precede blackwater-fever infection, yet there are many cases on record in which blackwater fever occurred before any kind of "malaria" had manifested itself. Plehn, Scott, Ritchie, Cardamatis, Lynch, Hearsey, Daniels, and others have reported cases of blackwater fever in robust individuals who were attacked within two or three months of their arrival in a blackwater-fever country. Officers in the African colonial service frequently relate that the attack of blackwater fever for which they were invalided suddenly developed while they appeared to be in perfect health and without any malarial antecedents. Daniels states that few cases occur during the first six months' residence, that they rapidly increase during the next six months, are most

Digitized by Google

numerous during the second and third year, and become rare after five years' residence. That is exactly what might be expected to happen with any localized infectious disease. The relatively small number of cases within the first six months may be explained by non-exposure to the causative agents of the disease; indeed, many arrive in the endemic district at the end of the epidemic season. The progressive prevalence of cases during the first three years finds an obvious explanation in the accumulating chances of infection; the decrease in the later years may be partly accounted for by the progressive diminution in the number of the older residents and by the weeding out of the most susceptible. Daniels states that the early cases of blackwater fever—those under one year's residence—are mainly (14 out of 21) in persons resident at or below the 1,500 feet level; and the majority (10 out of 14) of cases in persons having four years' residence are in persons residing principally in the highlands.

Exciting cause.—There are three theories as to the essential etiology of blackwater fever—1, the "malaria" theory; 2, the quinine theory; 3, the specific theory.

1. *The malaria theory.*—The prevalence of blackwater fever in malarious regions, the great frequency of its occurrence in persons who had previously suffered from one or other of the malarial fevers, the finding of malaria parasites and hæmozoin in the blood and organs, and the large mononuclear leucocytosis of hæmoglobinuric cases led to the belief that blackwater fever was an unusually severe form of "malaria." Against this theory is the fact that although blackwater fever is certainly co-endemic with one or other form of malaria in several regions, it is not so in all regions. It has its own peculiar distribution, and is absent or very rare in many places in which the various intermittent fevers are especially rife. It is exceedingly common amongst the few Europeans who live in tropical Africa; it is practically unknown amongst the many thousands of Englishmen who live in the fever haunts of India and elsewhere.

It is quite true that blackwater fever generally occurs in persons who have previously suffered or are suffering from malaria; but this does not prove that it is a special manifestation of malaria. It may be concurrence merely. We do not believe tuberculosis to be a peculiar manifestation of enteric fever because it often follows in the wake of that disease. Moreover, as already pointed out, blackwater fever frequently attacks people who previously had never had a single paroxysm of intermittent fever. The fact that malaria parasites are often found in the early stages of black-

Digitized by Google

water fever is not surprising when we consider that in many places malaria is exceedingly common and is co-endemic with blackwater fever. Although the benign tertian and quartan parasites have rarely been found in the blood of blackwater fever cases, the parasite which most frequently occurs is the subtertian, because it is that species of malaria parasite which is most common in the endemic regions of blackwater fever. Yet subtertian malaria differs in many clinical respects from blackwater fever. It is true that subtertian varies considerably in different cases; but the type of the disease does not alter, and the number and distribution of the parasites in the organs are generally in accordance with the intensity and nature of the various symptoms. On the other hand, cases of blackwater fever, however grave, however mild, always exhibit the same characteristic symptoms, with no difference other than as regards intensity and duration. Admitting the malaria theory of blackwater fever, we should have to consider a mild relapse of blackwater fever to be an unusually severe attack of subtertian—an untenable paradox. When malaria parasites are found in cases of blackwater fever they may be very scanty and in no way proportional to the symptoms of the disease. But in many cases no parasites are found; or, what is still more striking, if there were a few parasites before the attack, they invariably completely disappear with the onset of blackwater fever, and may not return after recovery from the latter disease. In analogy with what is sometimes observed in pernicious cases of subtertian fever, some authors have suggested that the parasites, though scarce or even absent in the peripheral blood, may be numerous in some internal organ, particularly the bone-marrow and spleen.

The discovery that severe cases of subtertian malaria may have a transient hæmoglobinuria, if the urine is examined spectroscopically, and the analogous and very rapid hæmolysis which takes place in pernicious malarial attacks, with the production of a similar hæmolytic icterus, rather strengthen the theory of their intimate association.

Much has been made of the large mononuclear leucocytosis present in this disease as a proof of its malarial nature. But we now know that a similar type of leucocytosis occurs in several other forms of protozoal disease.

If blackwater fever be caused by any one of the known malaria parasites, it may be a particular hæmolytic *strain* of the subtertian, or this parasite must have acquired its peculiarly powerful hæmolytic properties in a previous passage through an as yet unrecognized mammalian or insect host; or the subject of blackwater fever must

Digitized by Google

have been exposed to some specific influence present in blackwater-fever countries but absent in other malarial districts.

The work of Wade Brown has shown that liberation of alkaline hæmatín, which he regards as identical with malarial hæmozoin, into the plasma in itself causes an active hæmolysis of the red cells proportionately depending upon the amount of this pigment liberated by the parasite. More experimental work in this direction is desirable.

2. *The quinine theory.*—The quinine theory of blackwater fever arose in Greece. It was first suggested by Verétas in 1858, and soon became popular amongst Greek physicians. In 1874 it was upheld by Tomaselli in Italy, and more recently it received the support of Koch. The idea that quinine might produce blackwater fever originated from a misinterpretation of the fact that the administration of quinine, even in small doses, may provoke the manifestation of blackwater fever in a patient in whom the infection is latent. As quinine, even in toxic doses, never produces *blackwater fever* in healthy people or in malaria patients elsewhere (though a quinine hæmoglobinuria—quite a different condition, in persons with an idiosyncrasy for that drug—undoubtedly does exist), its peculiar action in Africa had to be explained by a peculiar hypothetical idiosyncrasy—an idiosyncrasy which, curiously enough, is found only in certain malarious countries and not in others. Thus, the connection between quinine and blackwater fever may not be one of cause and effect, but merely one of coincidence. Blackwater fever was known long before the introduction of cinchona bark into Europe, indeed it was known in the days of Hippocrates. Besides, even recently, numerous cases of blackwater fever have been reported amongst Europeans who had never taken quinine. Cardamatis mentions thirty-two such cases. Then, again, a number of physicians have administered quinine in large doses for the treatment of blackwater fever and have greatly vaunted its beneficial action. Quinine, in large doses, undoubtedly provokes in some the clinical manifestation of blackwater-fever infection. So, and probably much more powerfully, do chill and fatigue. But no one will contend that the latter cause this disease. Why then attribute it to quinine, which, logically, has no stronger claim ?

3. *The specific theory.*—In 1893, in a paper read before the Epidemiological Society, Manson stated that, on account of its peculiar symptoms and geographical distribution, he believed blackwater to be a disease *sui generis.* In 1898 Sambon suggested, because of the striking analogies that its distribution, course, symptoms, and morbid appearances have with the hæmoglobinuric

Digitized by Google

fevers of cattle, horses, dogs, and sheep, that blackwater fever might be a form of babesiasis. This view, which has been adopted by Blanchard and others, deserves consideration. It is quite reasonable to expect to find in man parasites belonging to this genus of the hæmoprotozoa, so abundantly represented amongst the animals most intimately associated with him. Certainly, of all the diseases of man of which the etiology is still obscure, none could be more appropriately ascribed to this group of parasites. The analogies between the hæmoglobinuric fever of man and the hæmoglobinuric fevers of cattle are most striking. To explain the fact that as yet no babesia has been found in cases of blackwater fever, it might be suggested that either the amœboid forms of the parasite have been mistaken for the early forms of the subtertian parasite, or that the parasite has escaped observation on account of diminutive size or anatomical habitat, or because it is not usually found in the peripheral blood.

It is well known that when cattle, natives of the South African endemic regions of Texas fever, are inoculated with rinderpest, they develop hæmoglobinuria and the other symptoms of Texas fever, from which disease they might be supposed to be pathologically immune. The blood of immune cattle in Texas-fever regions, we know, contains, in small numbers, the babesia. Edington's experiments show that the supervention of a second infection, rinderpest, determines the multiplication of the latent babesia and the explosion of the characteristic symptoms. May this not be in strict analogy with what happens in blackwater fever? The infection of blackwater fever may remain latent for considerable periods, until provoked into activity by some special agency, as cold, shock, quinine, or some additional infection, especially malaria.

Cook has placed on record five cases of blackwater fever in which an attack of spirillum fever appeared to be the provocative agent.

The probability is that particular persons infected with subtertian malaria are in a potential condition to develop blackwater fever, and that the exciting causes may be an overdose of quinine, cold (as in paroxysmal hæmoglobinuria), alcohol, over-exertion, or any secondary infection associated with a hæmolytic organism.*

Manifestly, the etiology of blackwater fever is not yet settled, and it is wise to preserve an open mind on this important subject.

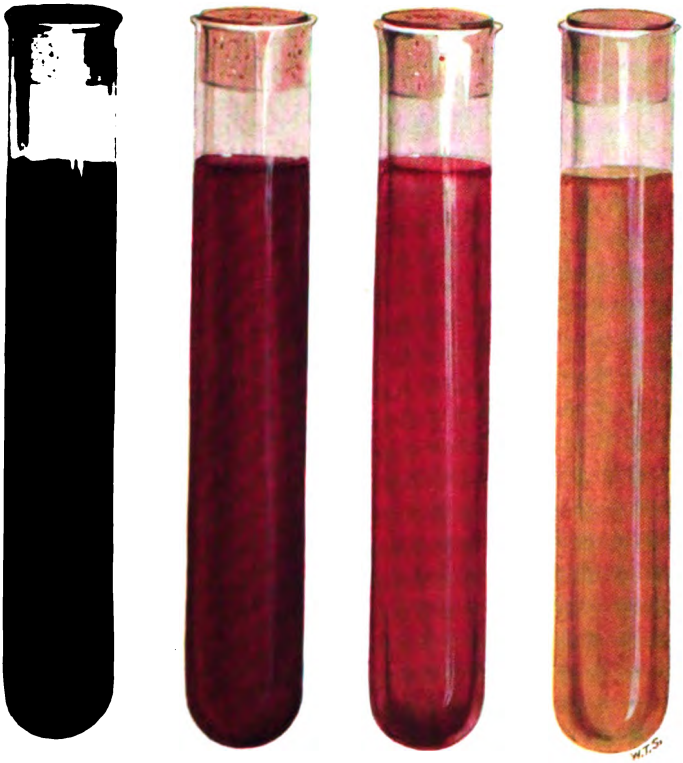
* A case which has come under notice developed blackwater after intramuscular quinine injection contaminated with *Bacillus welchii*. The subtertian malaria infection was of three weeks' duration, and was responding favourably to quinine-therapy. An acute hæmolysis supervened, with hæmoglobinuria, icterus and hæmatemesis, immediately after the injection.

Digitized by Google

Incubation period.—We know nothing definite as to the incubation period of blackwater fever. Scott, in British Central Africa, noticed that the attack usually occurred about eight days after exposure in certain low-lying districts. Arkwright and Lepper, in their series of cases, state that the maximal interval between the first recognized attack of malaria and the first attack of blackwater was ten years; the minimum, fifty days. That the disease may remain in abeyance for a considerable time is proved by the facts that recurrences after long intervals—months—are very common, in fact the rule; and that in some cases the first attack may manifest itself in Europe several months, and in one recorded case as long as five years, after the patient has left the endemic regions. Manson met with a case in England in which a severe attack, followed by a still more severe and prolonged relapse, was the first manifestation of a blackwater-fever infection that must have been acquired at least nine and a half months previously—the time that had elapsed since the patient left Africa. Similar cases have been seen by others.

Symptoms.—The onset of blackwater fever is usually sudden. A slight or, more generally, a very severe rigor is followed by intermitting, or remitting, or irregular fever with marked bilious symptoms. Earlier or later in the attack, usually during rigor, the patient becomes conscious of aching—perhaps severe—pain in the loins, in the region of the liver and spleen, which are enlarged and palpable, and over the bladder. In exceptional instances these local pains are absent. In consequence of a somewhat urgent desire he passes water, when he is astonished to see that his urine has become very dark in colour, perhaps malaga-coloured or, possibly, almost black. The fever continues, though not necessarily very high. Very likely he suffers from epigastric pain and distress, bilious vomiting to an unusual extent, and, it may be, bilious diarrhœa; or he may be constipated. The pain in the loins and the liver-ache continue; and the urine becomes darker and darker. By and by the sufferer breaks into a profuse sweat and the fever gradually subsides. The urine, which hitherto may have been very abundant, or perhaps somewhat scanty, now flows freely; and after passing through various paling shades, from dark brown to sherry red, becomes once more natural in appearance (Plate VIII.). Usually, and coincidently with the appearance of the dark colour in the urine, or even before this has been remarked, the skin and scleræ rapidly acquire a deep saffron-yellow tint. This icteric condition persists and even deepens during the progress of the fever, continuing for several days to be a striking feature

Digitized by Google



1 2 3 4

Fig. 1.—At acute stage, methæmoglobin and oxyhæmoglobin.
Fig. 2.—Stage of defervescence, preponderance of oxyhæmoglobin.
Fig. 3.—Further defervescence.
Fig. 4.—Stage of recovery, traces of methæmoglobin.

BLACKWATER-FEVER URINE.

(By permission of London School of Trop. Med.)

PLATE VIII.

Digitized by Google

Digitized by Google

in the symptoms. Occasionally bile-pigments are present in the serum; more usually free hæmoglobin can be demonstrated spectroscopically (Arkwright). When the fever subsides the patient is conscious of a feeling of intense weakness, from which he recovers but slowly. Fever, with or without rigor, may recur next day, or for several days; or it may cease; or it may be remittent, or almost continued, in type. The hæmoglobinuria may recur with each rise of temperature, or there may be only one or two outbursts; it may continue for an hour or two only, or it may persist off and on for several days or even weeks.

In the more severe form of hæmoglobinuric fever there is usually a very great amount of bilious vomiting, of intense epigastric distress, and of severe liver- and loin-ache. The urine may continue copious and very dark in colour; or, continuing hæmoglobinous, it may gradually get more and more scanty, acquiring a gummy consistence, a few drops only being passed at a time. It is considered that the kidneys may excrete up to 25 per cent. of the total hæmoglobin in the blood, though this by no means represents the total amount liberated in many cases of blackwater fever. Finally, urinary excretion may be completely suppressed.

In severe cases death is the rule. It appears to be brought about in one of three or four ways. The fever may assume the typho-adynamic type; or suddenly-developed cerebral, hyperpyrexial, or algid symptoms may supervene. Hiccough is said to be a fatal symptom. In other cases the symptoms may be like those consequent on sudden and profuse hæmorrhage—jactitation, sweating, sighing, syncope. Or it may be that suppression of urine, persisting for several days, terminates, as cases of suppression usually do, in sudden syncope or convulsions and coma. Or, more rarely, nephritis may ensue and the patient die from uræmic trouble three or four weeks after all signs of hæmoglobinuria and fever have disappeared.

Manson saw in London a case in which the fatal issue appeared to have been brought about by persistent hiccough (always a bad sign), hepatitis, and vomiting of blood.

The urine.—If the characteristic dark-brown, generally acid, urine of a hæmoglobinuric case be stood for some time in a urine glass, it will separate into two well-marked layers; an upper of a clear though very dark port-wine tint, and a lower—perhaps amounting to one-half or one-third of the entire bulk—of a somewhat brownish-grey colour, and consisting of a sediment in which an enormous number of hyalin and hæmoglobin tube-casts are to be found, together with a large quantity of brownish granular

Digitized by Google

material. Epithelium is also met with. Blood-corpuscles may be entirely absent, or very few in number. With the hæmoglobin there is also an escape of the serum-globulin of the blood, for the urine, in many cases, turns almost solid on boiling. The precipitated albumen carries down with it as it subsides the dissolved and suspended hæmoglobin, leaving a pale-yellow supernatant urine. For some days after the urine has regained a normal appearance it will still contain albumen, though in gradually diminishing amount. Spectroscopic examination gives the characteristic bands of oxyhæmoglobin, sometimes those of methæmoglobin or acid hæmatin. Bile-pigments may occasionally be detected by the ordinary tests.

Mortality.—This varies greatly in different epidemics, in the same and in different places, and even under the same treatment. Some cases are so mild and transient, amounting, perhaps, to a single emission of hæmoglobinous urine, with little or no fever, that they are unattended with risk; on the other hand, a practitioner may encounter a run of severe cases in which nearly all die. Some old residents in Africa have passed through ten or more attacks with impunity. In Southern Nigeria, in some years, and in Algeria it has been as high as 50 per cent. On an average the case-mortality in blackwater fever may be put down at about 25 per cent.

Post-mortem appearances. *The kidneys.*—If the kidneys of a case fatal at an early stage of the disease are examined, they are seen to be enlarged and congested, the tubules blocked with hæmoglobin infarcts, the cells laden with yellow pigment grains, and the capillaries most probably with a certain amount of malarial pigment. If the case survive for three or four weeks and then die of uræmia, the appearances are those of large white kidney.

The *spleen* is enlarged, congested, and usually contains malarial pigment.

The *liver* is enlarged, soft, of a dark-yellow colour. Microscopically it reveals evidence of cloudy swelling with a large amount of hæmosiderin in the liver cells. Hæmozoin may or may not be present.

The *gall-bladder* is filled with dark-green, almost black, viscid bile.

Diagnosis.—The diseases with which blackwater fever might be confounded are—1, paroxysmal hæmoglobinuria; 2, bilious remittent malaria; 3, yellow fever; 4, Weil's disease. If it be borne in mind that rigor, hæmoglobinuria, pyrexia, are all in evidence at the outset in blackwater fever, and also that blackwater fever

Digitized by Google

is acquired only in certain countries, an error in diagnosis is improbable.

As regards paroxysmal hæmoglobinuria occurring in the tropics, a diagnosis might be impossible. Both diseases have the same symptoms. Paroxysmal hæmoglobinuria, as a rule, is of a milder type. In bilious remittent malaria an examination of the urine will suffice to exclude one of the characteristics of blackwater fever, namely, the presence of hæmoglobin. Moreover, the malaria parasite will be present in the blood throughout the fever until quinine has been administered. In yellow fever the initial rigor is rarely severe, the appearance of icterus is a comparatively late event, the spleen and liver are not usually enlarged, the urine is albuminous, and if blood be present the erythrocytes are abundant. The same remarks apply to Weil's disease.

Treatment. — Having regard to the frequency with which hæmoglobinuric fever concurs with malarial infection, and the well-established fact that *quinine* may precipitate or determine a hæmoglobinuric attack, the question of the administration of that drug in hæmoglobinuria becomes an important point. Some practitioners of experience recommend the exhibition of the drug in heroic doses, giving it every two hours in divided doses to the extent of 120 gr. a day; this they keep up till convalescence is established. On the other hand, hæmoglobinuria may come on while the patient is cinchonized. The Plehns, Koch, and others, after trying quinine in these cases, and carefully comparing the results of treatment both with and without quinine, abandoned its use. So long as the hæmoglobinuria continued they treated the patient symptomatically, cautiously resuming the specific if the case merged into and concluded as a simple intermittent. There can be no doubt that in large doses quinine exercises a certain amount of destructive action on the blood-corpuscles, rendering their hæmoglobin unstable. When, therefore, its toxic influence is superadded to that of the specific cause of the hæmoglobinuric fever, it may be that it supplies the little that is required to determine an extensive liberation of hæmoglobin, which, had the quinine been withheld, might not have taken place. Bastianelli lays down the following sensible rules as to the use of quinine in hæmoglobinuric fever: (*a*) If hæmoglobinuria occurs during a malarial paroxysm and parasites are found in the blood, quinine should be given. (*b*) If parasites are not found in the blood, quinine should not be given. (*c*) If quinine has been already given before the hæmoglobinuria has appeared, and no parasites are found, its use should be suspended; but if parasites persist, it should be continued.

Digitized by Google

Recommendations.—Patients who are suffering from or are threatened with hæmoglobinuria, or who have had this disease before, on the slightest indication of fever should go to bed at once, keep the skin warm and scrupulously protected from draughts, and take plenty of warm fluid ; if parasites are present in the blood, moderate doses—5 gr.—of quinine every three or four hours (intramuscularly by preference) and a moderate dose of calomel should be given. Patients threatened with blackwater should not be moved, much less travel.

When the urine tends to be suppressed, diuretics must not be given with the idea of stimulating the kidneys. In these circumstances hot fomentations should be applied to the loins, plenty of bland diluents administered, and an exclusive milk diet ordered until all albumen has disappeared from the urine. Indeed, even in the mildest as well as the gravest cases, the free and frequent administration of fluid is a most important measure, whether the patient is thirsty or not, and should be insisted on from the beginning of the attack. When, owing to persistent vomiting, fluid cannot be retained by the stomach, enemata of warm physiological *salt solution* (much less irritating to the bowel, and thus far more likely to be retained than plain water) should be administered repeatedly, 6–8 oz. every half-hour or hour. If these are not retained, the salt solution (a teaspoonful to the pint of water), sterilized, may be slowly introduced into the subcutaneous connective tissue of the flank or elsewhere by means of a hollow needle attached by a rubber tube to some improvised reservoir placed one or two feet above the level of the patient. The water is rapidly absorbed, and cannot fail to be useful in washing out the hæmoglobin infarcts which plug the renal tubules and bring about, or at all events contribute to, suppression of urine. In cases with convulsions or coma, 5-per-cent. *glucose solution* given intravenously to the extent of two or three pints is advocated. Marked restlessness may require minute doses of *morphia* ($\frac{1}{10}$ gr.); but this drug, of great use at times, must be employed with caution. This is the only rational and safe systematic treatment of hæmoglobinuric fever. Antipyretic drugs, as antipyrin and phenacetin, are dangerous.

Transfusion of blood has been successfully practised in high degrees of anæmia in some cases. The blood of the donor should be drawn off, by means of a needle and rubber tubing, into a "Robertson's bottle" containing 160 c.c. of a 3·8-per-cent. solution of sodium citrate to prevent clotting. Blood up to 1,000 c.c. can be collected and stored in this way. The flask of citrated blood can be stood in warm water till run into the veins of the

Digitized by Google

recipient by the open method and given slowly. Whenever possible, attention should be paid to the choice of a suitable donor; he should belong either to Group IV. or to the same group as the recipient.*

One plausible objection to blood transfusion is to the effect that the added blood supplies additional hæmoglobin and involves additional risk of infarction of the renal tubules and suppression of urine.

Oxygen inhalations are indicated, but are rarely available. Intravenous injections of *hypertonic saline*, and also of *neosalvarsan*, have in certain cases been followed by recovery.

In desperate cases of suppression of urine, Stannus suggests, and has practised with temporary success in one case, incision of the capsule of the kidney.

Sternberg's mixture of bichloride of mercury and sodium bicarbonate (p. 205) has come into favour lately, especially in Central Africa.

Calomel in large doses—20 to 30 gr.—is with some a favourite remedy for hæmoglobinuric fever. Formerly it was used systematically in Africa in these cases; it has been given there by the teaspoonful, but cases recover perfectly without a grain of calomel or of quinine. Severe stomatitis may arise from the former; it should therefore be employed with great caution, and in reasonable doses.

Nursing is a most important element in the management of blackwater fever. If the stomach will retain food this should be given in a bland and fluid form, but there should be no attempt to force feeding, especially with rich and indigestible viands. One precaution against syncope must be sedulously enforced: the patient must not be allowed to sit up, much less to get out of bed, until food has been retained and assimilated, and the risk of sudden death from syncope has passed.

If possible, the subject of a hæmoglobinuric attack should quit the endemic area, and never return to it, or to any malarial locality; a severe attack, or a second attack, implying as they would special liability, should be regarded as imperative indications to this effect.

Prophylaxis.—All depressing and predisposing causes must be carefully avoided, more especially chill, fatigue, and malaria, and also, and especially, irregular dosing with quinine. In blackwater regions those who are the subjects of malarial infection should take quinine systematically, never irregularly, and should

* *See* Keynes, *Lancet*, June 5, 1920, and Fleming and Porteous, *ibid.*, June 7, 1919.

Digitized by Google

be especially careful to continue its use, in the accustomed doses and at the accustomed intervals, for at least six months after arrival in Europe. Most of the cases of blackwater seen in this country are attributable to neglect of this precaution and to a big dose of quinine taken for a relapse of a malarial infection supposed to have died out. Those who have had blackwater should gradually habituate themselves to quinine, beginning with minute doses —$\frac{1}{2}$ gr.—slowly increased to 5 gr., which dose they should take daily while under the endemic influences, and at least for six months afterwards.

The experienced practitioner should be on his guard to treat malarial cachexia from the West Coast of Africa seriously, especially if the skin is icteric, the spleen and liver enlarged, the urine highly coloured, albuminous, containing urobilin, and scanty, whether subtertian parasites are found in the blood or not, for these signs are all suggestive of a threatened attack of hæmoglobinuria.

Digitized by Google

CHAPTER VII

TRYPANOSOMIASIS OF MAN*

Definition.—Morbid conditions produced by parasites belonging to the genus *Trypanosoma*, including irregular chronic fever, skin eruptions, local œdema, adenitis, physical and mental lethargy, and, in a large proportion of cases, death.

History.—Although its true etiology was not apprehended until comparatively recently, sleeping sickness, the terminal phase of African trypanosomiasis, has been known for over a century.

The occurrence of trypanosomes in animals has been recognized for at least sixty years, first in cold-blooded vertebrates, later in mammals. The best-known and first-described mammalian species is that of the rat (*Trypanosoma lewisi*). It was discovered by Lewis, in 1879, in Calcutta. In the following year Evans described a similar parasite (*T. evansi*) in the blood of horses in India ; he found that it also infects camels, elephants, buffaloes, and dogs, and that it is the cause of the disease called " surra," which, from time immemorial, the natives of India have ascribed to the bite of certain blood-sucking flies. Fifteen years later Bruce showed that nagana, the " fly disease " of horses, bovines, and other species of domestic mammals in Africa, is due to the same kind of organism (*T. brucei*). Since these discoveries were made, trypanosomes have been found in many species of mammals, as well as in numerous birds, fishes, and reptiles. Though differing in degree of virulence, they all, at least in mammals, give rise to more or less similar types of disease.†

In 1890 Nepveu, in the course of researches in Algeria on malaria, encountered these protozoa in the blood of man. He appears to have been the first to do so ; but, unfortunately, his original description is vague and his illustrations are crude. He established no definite relationship between the organisms he alluded to and the associated morbid conditions ; consequently, his observations did not receive the attention their significance deserved, although, later, he emphatically affirmed that a trypanosome had to be reckoned with as a factor in human tropical pathology.

* Laveran and Mesnil in their " Trypanosomes et Trypanosomiases, 1912," have given a very complete and accurate account of this subject. For fuller details the student is referred to this work.

† For a brief description of the trypanosomes of mammals, *see* pp. 759-64.

Digitized by Google

In 1901 Forde encountered a flagellated parasite in the blood of a European suffering from an irregular non-malarial fever, in the River Gambia Colony. This parasite he showed to Dutton (1902), who recognized it to be a trypanosome. Later, Dutton found a similar organism in the blood of a native of the same colony, and suggested the name *T. gambiense*, which the parasite now bears. Subsequently many cases were described, both in Europeans and natives, and the association of the parasite with a peculiar form of febrile cachexia was quickly and satisfactorily established.

A great impulse was given to the study of the subject by the discovery of trypanosomes in the cerebro-spinal fluid as well as in the blood of cases of sleeping sickness, by Castellani in Uganda, in 1902. Castellani's suggestion that the parasite is the cause of sleeping sickness has been fully confirmed by Bruce, Nabarro, and other investigators, who have also shown that in Uganda the tse-tse fly, *Glossina palpalis*, is the transmitter of the infection, an hypothesis already advanced on analogical and epidemiological grounds by Sambon and Brumpt. Then (1909) came the important discovery by Kleine that the tse-tse fly was no mere mechanical transmitter of the trypanosome, as had been supposed, but was a true intermediate host. Later, on morphological and clinical grounds, Stephens and Fantham established the existence in Rhodesia of another species or variety of trypanosome (*T. rhodesiense*), which Kinghorn and Yorke have since proved to be transmitted by *Glossina morsitans*.

Macfie has recently described another subspecies of trypanosome, *T. nigeriense*, said to be less virulent than *T. gambiense* and transmitted by *Glossina tachinoides;* and on inoculation into animals it is said that many short stumpy forms are produced.

Meanwhile Chagas has associated a disease, occurring in Brazil, with a peculiar species of trypanosome, *Schizotrypanum cruzi*, having a special transmitter, *Conorhinus megistus*. (*See* p. 138.)

Trypanosoma gambiense

Geographical distribution.—The presence of *T. gambiense* has been definitely ascertained for the west of Africa from the Senegal in the north to Mossamedes and the upper reaches of the Lualaba in the south. Also in the Niger and Congo basins, and in Uganda, where it must have been introduced only recently, apparently about the end of the nineteenth century. Throughout this vast area the infection is not uniformly distributed. It occurs in a patchy way, principally along the banks of the rivers and the shores of the lakes, conformably to the distribution of certain

Digitized by Google

tse-tse flies, and apparently influenced also by the frequency and nature of the intercourse and by the occupations of the inhabitants. There is strong reason for believing that the recent influx of Europeans into tropical Africa and the consequent increased movement of the natives is spreading the disease, and that this extension has by no means reached its limit. As regards the eastern side of the continent, the disease has not extended much beyond the shores of the Victoria Nyanza. In this locality its present limits are Kajo Kaji, about the 4th degree N. parallel of latitude, on the Nile to the north, and stretching inland to the southern and western portions of the Bahr-el-Ghazal province and the southern end of Lake Tanganyika to the south. There is every reason to apprehend that, in time, the distribution of trypanosomiasis will become coextensive with that of the appropriate tse-tse flies.

Etiology.—In common with other trypanosomes, *T. gambiense*, as seen in fresh blood, is an active, wriggling organism, having a spindle-shaped body which is slightly compressed laterally and spirally twisted. It is provided with a delicate, wavy membrane —the *undulating membrane*—which fringes the convexities of the body, and terminates anteriorly in a free, whip-like filament, the *flagellum*. Suitably stained specimens show a *trophonucleus* about the centre of the body, and a minute, deeply staining chromatin mass, the *kinetonucleus*, generally near one pole. The extremity of the body which encloses the kinetonucleus is regarded by all authorities as the *posterior extremity;* it varies greatly in shape and may be pointed or obtuse. The opposite end, the *anterior extremity*, tapers to a point, to which the flagellum is attached. The flagellum arises at the posterior end from a minute basal granule, or end-knob, the *blepharoplast*, in relation to which there is the small "chromatin"-staining rod-like or spherical body called the *kinetonucleus*. Between the two there is sometimes a vacuole (Fig. 43). The flagellum passes forwards along the body from its point of origin and forms the edge of the undulating membrane, before it finally emerges at the anterior end of the free flagellum. In certain specimens the cytoplasm is homogeneous; in other specimens comparatively faintly staining granules are visible. In comparing and measuring a large series of specimens it becomes apparent that there is great diversity in the dimensions of the body of the parasite, the nucleus, and the flagellum (Fig. 43). Thus, some are short and stumpy, with short or no flagellum, measuring from 14 to 20 μ in length; others are long and slender —23 to 33 μ; others again are of intermediate dimensions—20 to 24 μ in length by 1·40 to 2 μ in breadth.

Digitized by Google

In certain instances evidences of multiplication by longitudinal division are seen (Fig. 44). The process commences most frequently in the kinetonucleus, which elongates and then divides. The nucleus divides almost simultaneously, sometimes before the kinetonucleus. The division of the kinetonucleus is followed by the duplication of the thickened margin of the undulating membrane, beginning at its blepharoplast attachment; this, in its turn, is followed by longitudinal division of the whole body. According to Miss Muriel Robertson—the accomplished protozoologist who has worked in Uganda—only a portion of the flagellum is split off with the daughter individual. The fission of the body is effected dorso-ventrally, but the resulting forms do not separate along the ventral border until the new flagellum has appeared, the final separation proceeding antero-posteriorly; parasites still adhering by their posterior extremities are occasionally encountered. The division forms are usually of about equal size, and slightly smaller than the parent form.

Crithidia-like forms have been found in the cerebro-spinal fluid and, according to Breinl and Fantham, latent encysted forms in the lungs, spleen,

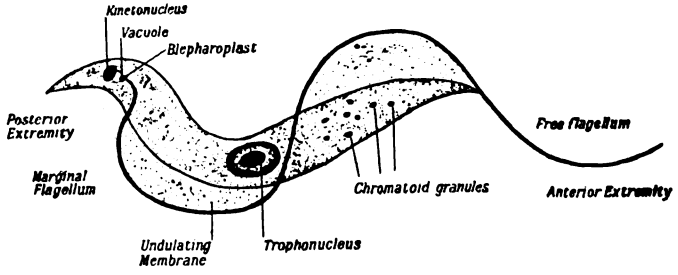


Fig. 43.—Schema of trypanosome. (*After Dobell.*)

and bone-marrow. Granule-shedding, similar to that described by Balfour in pathogenic spirochætes, has been observed by Fry and Ranken in the liver, spleen, bone-marrow, and lymphatic glands. Wolbach and, later, Stevenson have shown that in experimental animals trypanosomes are found in all organs, including the brain, and that they are distributed throughout the tissues outside the blood-vessels.

Although we are accustomed to observe the parasites in the blood, there is reason to believe that this is not their only or principal habitat. As suggested by Mott, and proved by Greig and others, they are generally more easily found in the lymphatic glands, which are often markedly enlarged. They occur also in the cerebro-spinal fluid, and probably in the fluid of the serous cavities—facts pointing to the lymphatic system as an important habitat of the trypanosoma. As regards the blood, there is no uniformity in the number of parasites present: sometimes they are fairly abundant, one or two in each field of the microscope; at other times and in the same patient it may be difficult or

Digitized by Google

impossible, even after prolonged search, to find a single specimen; in some instances they tend to recur cyclically at intervals of a week or more. On the whole, although this is by no means invariably the case, the parasites are most abundant in the blood during the febrile attacks to which these patients are so subject.

Formerly many attempts were made to cultivate *T. gambiense* on artificial media, but without marked success, notwithstanding that the parasite is readily communicated to monkeys, dogs, rats, guinea-pigs, and many other animals, though amphibia and reptiles

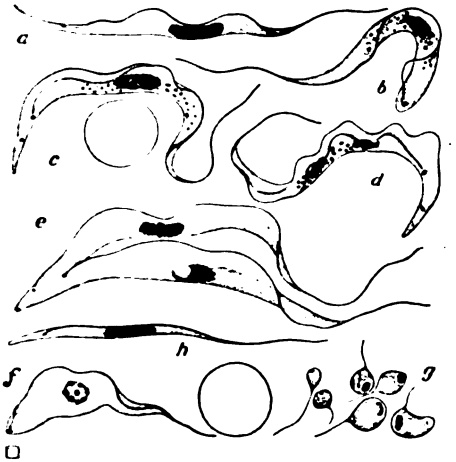


Fig. 44.—Trypanosoma gambiense: various forms from blood and cerebro-spinal fluid.

a, Elongated posterior extremity; *b*, blunt ditto; *c*, *d*, and *e*, dividing forms; *f* and *h*, probably sexual forms; *g*, small round forms from cerebro-spinal fluid.

are immune. Success was not attained till a suitable medium, termed the N.N.N. medium (p. 894), was discovered.

On this medium Novy and McNeal have shown that *T. lewisi* and other trypanosomes multiply rapidly in the water of condensation, and that in many species subcultures can be carried on through an indefinite number of generations. Thus, *T. gambiense* has been cultivated for four generations; *T. rhodesiense* is more difficult to cultivate. Unfortunately, *T. gambiense* is usually somewhat refractory and does not multiply readily in this culture medium. In such cultures, however, the trypanosome form may be lost, the flagellum springing directly from the anterior extremity and no undulating membrane developing. Cultivation can now be utilized

Digitized by Google

as a diagnostic method of demonstrating trypanosomes, if very scarce in the peripheral blood.

Interesting observations have been made by Laveran and others on a very striking phenomenon exhibited by trypanosomes, in certain circumstances, both in the blood and in artificial cultures. Upon the advent of unfavourable biological conditions in these media, such as the influx of serums of non-susceptible animals, increasing scarcity of nutriment (as in the alimentary tube of an appropriate

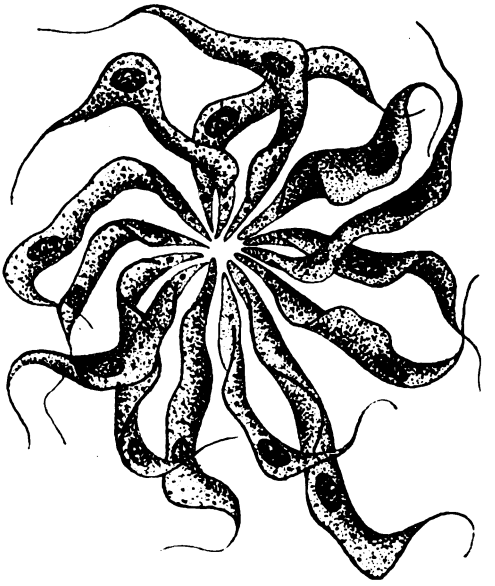


Fig. 45.—Agglomeration of Trypanosoma lewisi in the defibrinated blood of an immunized rat. (*After Laveran.*)

invertebrate host), lowering of temperature, or the addition of chemical solutions to artificial cultures, the trypanosomes tend to congregate in bunches in which the posterior extremities of the parasites are opposed, the flagellated extremities remaining free (Fig. 45). One such group is termed a " primary " agglomeration, and may be composed of upwards of a hundred individuals. In many cases these primary clusters themselves become grouped together to form still larger tangled masses known as " secondary " agglomerations. Agglomeration does not of itself seem to have any ill effect on the constituent parasites, which may again disperse, apparently quite unaltered. Sometimes all the individuals forming

Digitized by Google

a cluster become disagglomerated; at other times the break-up is only partial, a certain number of the more feeble and less mobile parasites remaining together and slowly dying. The significance of this phenomenon has yet to be ascertained. Some authors believe that it indicates a recuperative molecular interchange between the associates.

In cultures, in many instances, trypanosomes acquire a spherical form and undergo multiple division. They lose their flagella in the process, certain of the division forms subsequently acquiring such an organ, which now invariably springs, as already mentioned, directly from the blepharoplast. These culture forms possibly represent a stage in the life of the parasite which, in normal conditions, is passed in the vertebrate host or, more probably, in the insect host.

How long a trypanosome infection may persist in the human body has not been definitely determined, but there is direct evidence that it may continue for several—three or four—years. From what we know of the incubation period of sleeping sickness it is not improbable that this period is sometimes greatly exceeded, and may extend to seven years or longer.

Extrusion of granules and their further development.—Fry and Ranken described under this title a remarkable phenomenon. Balfour has described a similar process in spirochætes. It is especially observable in those more chronic forms of trypanosomiasis of man and animals in which the trypanosomes disappear from the blood for considerable periods at a time, and may explain the occasional infectivity of blood in which the parasite cannot be detected with the microscope.

The observers referred to state that trypanosomes may or may not contain two kinds of granules, one kind being of the nature of food material; the other, which is a sharply defined refractile body, is extruded, and in process of time becomes transformed into another trypanosome. This evolution is especially noticeable in *T. gambiense*, but they have witnessed a similar process in other species of trypanosomes.

Rôle of the tse-tse fly.—An important practical point is the question of the transmission of the parasite. As already mentioned, the well- and long-known rôle of the tse-tse fly* in the transmission of the trypanosome of nagana suggests that the corresponding parasite of man is transmitted by a corresponding insect—a suggestion borne out by considerations of distribution and by experiment.

Minchin, Gray, and Tulloch have shown that when *Glossina palpalis* was half-fed on a rat infected with the cattle trypanosome of Uganda (probably *T. brucei*), and immediately transferred to

* For a brief description of the tse-tse flies, *see* p. 143.

Digitized by Google

complete its meal on a healthy rat, in four out of five experiments the healthy rat contracted the infection; but if the transference was delayed, for an hour even, the experiment failed. A similar experiment with other blood-sucking flies (*Stomoxys*, for example) which, apparently, have no biological connection with *T. brucei*, succeeded to some extent. As such a method of feeding can only occur exceptionally in nature, it is reasonable to infer that the closely allied *T. gambiense* is not usually communicated in this purely mechanical way. We know that the malaria parasite can be communicated by the direct inoculation of malarial blood, but it is universally admitted that direct inoculation is not the natural method of transmission. The idea that the glossina inoculated trypanosomes in this direct way originated, undoubtedly, with the interpretation that has been placed on Bruce's experiments with nagana, an interpretation which may be incorrect. It is true that both Bruce and Minchin communicated trypanosoma infection to monkeys and other animals by means of tse-tse flies caught in the jungle. It is manifest, however, that before these tse-tse flies could have fed on the experimental animals an interval of many hours must have elapsed since their previous blood-feed. Therefore, in view of Minchin's failure to communicate the disease by insects that had been kept for only a short time after being fed on trypanosoma-infected animals, it is reasonable to conclude that there could have been no direct inoculation by these jungle-caught flies.

A more probable interpretation of the experiments, and one based upon what we know of the transmission of other hæmo-protozoa, is that the glossina serves as an alternative host in a truly biological sense, and not as a simple mechanical transmitter; that the trypanosome, after entering the intestinal canal of the insect (Fig. 46), undergoes developmental changes requiring a considerable space of time for their completion—developmental changes which enable it subsequently, when the opportunity occurs, to effect a lodgment in the human or other vertebrate host. That this view of the rôle of the tse-tse fly is correct has been established by Kleine, who, after feeding *G. palpalis* on animals infected with *T. brucei*, set the same flies to bite fresh animals at various intervals. Up to twenty (possibly sixteen) days the flies failed to convey the infection, but from that period onwards to the forty-seventh day, when the experiment concluded, they communicated the trypanosome to eight animals. Bruce and others have confirmed Kleine's results, and have ascertained that they apply to *T. gambiense* and other trypanosomes. It is estimated that 0·03–0·34 per cent. of

Digitized by Google

wild *G. palpalis* in Uganda are infective; but in captivity, if fed on trypanosome-infected blood, 5–6 per cent. of flies become infective, and, according to Miss M. Robertson, a still greater proportion (21 per cent.) if the flies are starved after feeding. More recently Bruce and his co-workers have found that in Nyasaland 1·35 per cent. of all wild tse-tse flies are infected with one or other of the disease-producing trypanosomes. It is to be noted that the trypanosome at intervals, not as yet ascertained, is incapable of infecting the fly. For this observation also we are indebted to Miss M. Robertson.

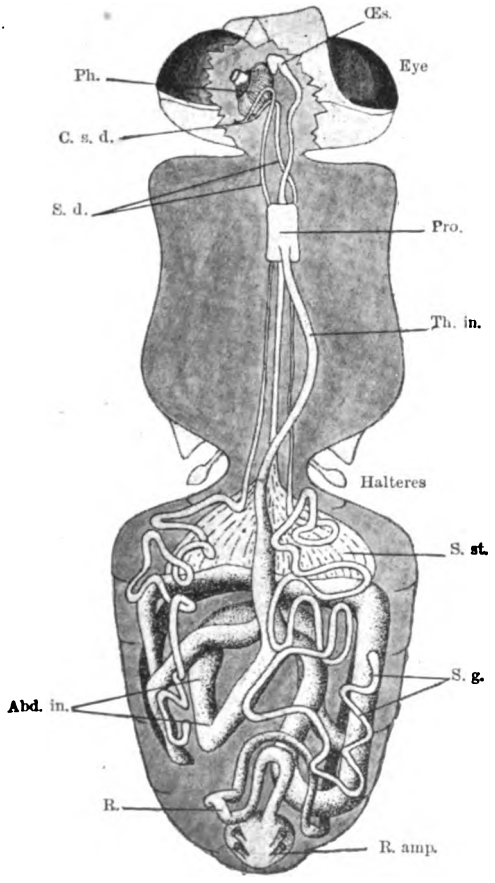


Fig. 46.—General view of digestive tract of Glossina palpalis. (*After Minchin, Report on Sleeping Sickness to the Royal Society,*)

Ph., pharynx; Œs., œsophagus; C. s. d., common salivary duct; S. d., salivary ducts; Pro., proventriculus; Th. in., thoracic intestine; S. st., sucking stomach; S. g., salivary glands; Abd. in., abdominal intestine; R., rectum; R. amp., rectal ampulla.

The trypanosome-infected contents of the stomach of a glossina, if injected into a susceptible animal, do not communicate the infection, although the parasites may be alive at the time of the injection. Possibly the multiplying forms in the stomach are of the same sexual nature as those of malaria in the mosquito—gamete forms—and therefore incapable of multiplication in a vertebrate host. Koch for *T. brucei*, and Minchin, Gray, and Tulloch for *T. gambiense*, stated positively that the parasites show

Digitized by Google

marked sexual differentiation within the stomach of the insect host.

The discovery by some of the above-mentioned investigators that jungle-caught tse-tse flies harbour a variety of species of trypanosome "wild forms," while only a small proportion of them convey *T. gambiense* (sometimes as many as a thousand of these insects were required before a successful infection of monkeys was obtained), makes it evident that extreme precision and care must be observed in order to eliminate sources of fallacy. That the tse-tse fly conveys the trypanosome is certain, and Koch's observation that trypanosoma forms may sometimes be observed in the blood-free droplet of clear fluid which can be expressed from the proboscis, as well as the conditions observed in experimenting, indicate that the infection is conveyed by the bite of the fly. But, even assuming that glossina has been proved to be the proper transmitter of *T. gambiense*, much remains to be done; the history of the trypanosome, from the time of its removal from one vertebrate by the glossina to its introduction into another vertebrate, has not been completed.

Minchin, having discovered encysted developmental forms of trypanosomes in the lower gut of the tse-tse fly, conjectured that the infection might be transmitted by the droppings when swallowed by man or other vertebrates. Further observation has not supported this conjecture.

Dealing with the entire life-history of *T. gambiense*, Miss Robertson summarizes her conclusions as follows:—

"1. *T. gambiense* undergoes an endogenous cycle of development in the vertebrate in the circulating blood. This cycle is of irregular duration and is repeated many times in the course of the disease.

"2. The short forms may be regarded as the adult blood-types; the intermediate types are growth-forms, proceeding to the long individuals, which are those about to divide. The products of division give rise, directly or indirectly, to the adult forms. The adult forms appear to be alone responsible for carrying on the cycle in the transmitting host.

"3. The multiplication occurs in the circulating blood.

"4. Multiplication of the parasites was never found within the cells of the liver, spleen, or lungs in monkeys.

"5. Rounded non-flagellate types were found on one occasion in the lung, liver, and spleen of a virulently infected monkey. They appear for the most part to be destined to destruction, but it is not excluded that they may survive in small numbers as latent forms.

"6. In the fly the trypanosomes are first established in the posterior part of the midgut. Multiplication occurs and trypanosomes of very varying sizes are produced.

"7. From the tenth or twelfth day onwards slender long trypanosomes are to be found in increasing numbers. These finally move forwards to the

Digitized by Google

proventriculus and are the dominant, though not the only, type seen there. The proventriculus becomes infected, as a rule, between the twelfth and twentieth days.

"8. The salivary glands become infected by the slender proventricular types. They reach the salivary glands by way of the hypopharynx; arrived in the gland, they become attached to the wall and assume the crithidial condition. Multiplication occurs, and finally small trypanosomes are produced, closely resembling the blood type. The passage through the crithidial stage is characteristic of the salivary development, and the trypanosome forms just mentioned are derived from the crithidial types. The development in the salivary gland takes from two to five days before the forms are infective.

"9. The fly is never infective until the glands are invaded. Trypanosomes from the proventriculus, when injected into a monkey, never produce infection. Trypanosomes may be found in the salivary glands as early as the sixteenth day of the cycle. An early infection of the salivary glands is always preceded by a very virulent and rapid gut infection.

"10. The trypanosomes are never attached to the wall of the alimentary canal, and there is no intracellular multiplication in the gut cycle. A crithidial stage does not occur in the gut cycle. The trypanosomes are never found in the body cavity, nor are they ever established in the rectum.

"11. Conjugation has not been observed, nevertheless the fly cycle as a whole has the biological significance of conjugation."

Considering the bionomics of glossina, it seems not improbable that some of the trypanosomes, after undergoing certain unknown changes, may enter the larva, and be thus transmitted by heredity to the vertebrate host. This has been suggested by Sambon. So far, however, such hereditary transmission has not been established. Yet it may be pointed out that it would conform in a remarkable manner to the habits of the piroplasms in relation to their invertebrate transmitters.

To settle these and other questions of great practical importance in connection with the rôle of the tse-tse fly in trypanosomiasis, experiments with laboratory-reared insects are indispensable; and, further, observations should be extended to all the species of the genus. We have no assurance that *Glossina palpalis*, *G. morsitans*, and *G. tachinoides* are the only efficient transmitters. Direct infection through breaches of surface or through mucous membranes (e.g. during coitus, as has been suggested by Koch) cannot be entirely excluded as a possibility.

Predisposing causes.—Neither age, sex, occupation, nor race *per se* has any influence on the susceptibility to trypanosoma infection, except in so far as they conduce to opportunity. Thus occupations (boatmen, fishermen, water-carriers) which imply a frequenting of the waterside haunts of the glossina conduce to infection.

Incubation period.—The incubation period of the glossina-

Digitized by Google

conveyed disease and that resulting from direct artificial inoculation seem to be about the same, from two to three weeks—in the case of dogs, horses, and monkeys. As regards man, observations are too few to warrant anything like a definite statement on this point, but in one or two instances circumstances seem to point to a similar incubation period.

Symptoms.—Without being too definite on the point, and basing the statement on the experience of a limited number of cases, it is suggested that the bite of an infected glossina is followed, in a proportion of cases, by a degree of local irritation of greater or less severity. This subsides in the course of a few days, to be followed, sooner or later, by fever, which may last a week or longer, and may be accompanied by the appearance, in Europeans at all events, of a peculiar type of erythema and a certain amount of serous infiltration of the connective tissue. A form of hyperæsthesia, known as "Kerandel's symptom," is usual, though not invariable; if the patient strikes a limb against any hard object, a degree of discomfort amounting to actual pain is experienced, the sensation being slightly delayed. In time the fever subsides more or less completely, to recur at irregular intervals of days or weeks. The fever is sometimes mild, sometimes severe, and occasionally hyperpyrexial (106·6° F.), the evening temperature being always the highest. The fever may last for weeks; the apyretic period may be equally prolonged. On the other hand, the fever may be continuous, or the apyretic period may last for months. Irregularity of degree and duration is a feature of the fever and, also, of the other clinical manifestations of trypanosomiasis. In time the patients become debilitated, anæmic, feeble both intellectually and physically. Headache is very often complained of. The heart's action is generally rapid and easily excited. The cervical glands and the glands of other parts of the body enlarge and may become tender. It may be that only one gland is visibly involved, or there may be a recognizable general polyadenitis, including the abdominal glands. The implicated glands may be very prominent, or they may not be easily felt. In the early stage of the infection they are soft, later they are indurated. Sometimes they are painless, sometimes distinctly painful and tender, rarely suppurating. This condition of irregular fever, of debility, of polyadenitis, of slight anæmia, may go on for months, or even in some instances, for years.

There is reason to hope that in a proportion of cases the disease may terminate at this stage. Manson saw three cases in which after many months of illness the symptoms entirely disappeared,

Digitized by Google

and were absent for several years, during which the parasite could no longer be found in the blood, whether tested by microscope or by animal injection (two cases). But, considering that the disease may present at various stages periods of quiescence which, in some instances, may be very prolonged, it would be rash to say whether in any instance of apparent recovery we are dealing with a radical cure, or merely with one of these long periods of latency. Experiments and observations by Laveran and others in other forms of trypanosoma infection, as well as cases of the disease in Europeans, justify the belief that occasionally the parasite does die out, either spontaneously or as a result of treatment.

It would appear that in a given area and in a given population there is a tendency for the virulence of the local trypanosome to decrease with lapse of time. Thus, the trypanosome of Southern Nigeria (now known as *T. nigeriense*), where sleeping sickness presumably has been long endemic, is less virulent and much more amenable to treatment than that of Uganda, where it is of quite recent introduction.

Remarkable features of human as well as of animal trypanosomiasis are the skin affections and the local œdemas. In many of the lower animals affected with their special trypanosomes, in addition to fever and physical lethargy, papular and pustular eruptions are not uncommon; and in man, especially in negroes, an exceedingly itchy papular eruption is a common symptom. In the European, and possibly in the negro—but in the latter, in consequence of his colour, not so evident—extensive skin areas are affected with a fugitive, patchy, frequently annular erythema (Fig. 47), usually most evident on the chest and back, but also very often on the face, legs, and elsewhere. This erythema seems to occur most frequently and most distinctly in the earlier stages of the infection. Some of the patches may extend to six inches or even to a foot in diameter, their margins fading off insensibly into the surrounding normal skin. Sometimes the erythema takes the form of large rings, occasionally complete, more frequently interrupted and irregular. Erythema nodosum sometimes occurs. Pressure or any irritation of the skin gives rise at once to transient congestion from vaso-motor paralysis of the skin capillaries.

In some of the lower animals a usual feature is œdema of certain parts of the body, especially the sheath of the penis, the under surface of the abdomen, and the neck. Similar though less extensive œdemas occur in man, in whom they are most apparent in the face and about the site of the erythema. In many instances there is a general fullness of the features, which, together with concomitant

Digitized by Google

flushing of the face, is apt to convey a false impression of sound health.

Neuralgic pains, cramps, formication and paræsthesiæ of different kinds are not uncommon. In two of Manson's European cases recurring orchitis, accompanied by an increase of parasites in the blood, was a feature. Painful local inflammatory swellings,

Fig. 47.—Rash of human trypanosomiasis. (*Photo: R. McKay.*)

which after a time subside without suppuration, have been seen in three cases; periostitis of tibiæ once. A toxic irido-cyclitis and choroiditis and deep œdema of the lower eyelid are sometimes met with.

In most cases the spleen is enlarged, sometimes enormously so, the swelling fluctuating with the fever. The liver also may be enlarged. As the patients affected with trypanosomiasis are usually the subjects of malarial disease, it is not always possible

Digitized by Google

to say whether the splenic enlargement is entirely or partly attributable to the trypanosome.

According to Greggio, trypanosoma infection is not, as a rule, transmitted to the fœtus; nevertheless, the abortion-rate in the infected is increased from the normal 7 per cent. in Congo natives to 31·7 per cent., and the infant mortality from 29 per cent. to 50 per cent.

Death from intercurrent disease, or from rapidly developing cerebral implication causing convulsions, the status epilepticus, coma, etc., may supervene at any stage of trypanosomiasis. Usually the case gradually drifts into the stage known as "sleeping sickness." * The incubation period may be a long one; among the slave-traders a period of seven years was regarded as being the limit.

Sleeping sickness. — The condition known as sleeping sickness may be regarded as the terminal stage of trypanosoma infection. Sometimes it exhibits acute features, sometimes it is exceedingly chronic. While in a proportion of instances an interval of many years, possibly seven, may elapse from the commencement of the infection to the development of this terminal stage, in the majority of cases the march of events is much more rapid. The characteristic terminal symptoms depend on implication of the nervous system either by the parasite itself or by its toxins.

According to Low and Castellani, the average duration of this stage of trypanosomiasis in the African is from four to eight months, not infrequently less; very chronic cases with a course of more than a year's duration are rare. Other observers refer to cases running on for three years, or even longer, and presenting occasionally temporary ameliorations.

Generally the first indications of the oncoming of sleeping sickness are merely an accentuation of the debility and languor usually associated with trypanosoma infection. There is a disinclination to exertion; a slow, shuffling gait; a morose, vacant expression; a relaxation of features; a hanging of the lower lip; a puffiness and drooping of the eyelids; a tendency to lapse into sleep or a condition simulating sleep; a slowness in answering questions; a shirking of the day's task. Dull headache is generally present. Later there may occur fibrillary twitching of muscles, especially of the tongue, and tremor of the hands, more rarely of the legs, indicating a definite implication of the motor centres.†

* It is customary to state that the development of the sleeping-sickness stage in trypanosomiasis concurs with and is dependent on the entrance of the parasite into the cerebro-spinal canal.

† In German East Africa, out of 55 patients in the last stages of the disease only 5 had sleep symptoms. Exophthalmos was noted 16 times.

Digitized by Google

By this time the patient has taken to bed, or he lies about in a corner of his hut, indifferent to everything going on around him, but still able to speak and take food if brought to him. He never spontaneously engages in conversation or even asks for food. As torpor deepens he forgets even to chew his food, falling asleep perhaps in the act of conveying it to his mouth, or with the half-masticated bolus still in his cheek. Nevertheless, such food as he can be got to take is digested and assimilated. Consequently, if he is properly nursed, at this stage there may be no general wasting. As time goes on he begins to lose flesh, tremor of hands and tongue becomes more marked, and convulsive or choreic movements may occur in the limbs or in limited muscular areas. Sometimes these convulsions are followed by local temporary paralysis. Sometimes there is rigidity of the cervical muscles and retraction of the head. Bedsores tend to form; the lips become swollen, and the saliva dribbles from the mouth. Gradually the lethargy deepens, the body wastes, the bedsores extend, the sphincters relax, and finally the patient dies comatose or sinks from slowly advancing asthenia. Possibly he succumbs to convulsions, hyperpyrexia, pneumonia, dysentery, or other intercurrent condition.

The manifestations described are subject to considerable variations. Mania is not uncommon; delusions may present themselves, or psychical and physical symptoms not unlike those of general paralysis of the insane are developed.

During the whole course of the nervous stage of trypanosomiasis the other symptoms already described as characteristic of the infection may be in evidence. The knee-jerks, though lost towards the end, are active at first; the fundus oculi is normal; the sphincters, until towards the end, are controlled; the urine is normal, and the bowels, although generally tending to constipation, act with more or less regularity.

Mortality.—Although spontaneous recovery may take place in the early stages of trypanosomiasis, when the disease has arrived at the stage of sleeping sickness death, it is believed, is inevitable. Corre has told us how native villages in Senegambia have been depopulated. What has occurred on the Congo, in Angola, and recently in Uganda, bears out this estimate of the gravity of the disease when it appears in epidemic form. We know that many islands on the Victoria Nyanza have been completely depopulated; and if it be true for a large part of the country, as Bruce has shown to be the case at Entebbe and its neighbourhood, that 30 per cent. of the population harbour trypanosomes, the

Digitized by Google

outlook for Uganda and neighbouring countries is grave indeed. The population of the implicated districts of Uganda, originally about 300,000, was reduced in six years to 100,000 by sleeping sickness.

Morbid anatomy (Fig. 48).—No gross lesions of the nerve centres, or of any other organ, have been described as invariably present; but in every case indications, principally microscopical, of an extensive meningo-encephalitis can be demonstrated. In a proportion of instances congestion of the meninges, effusion of

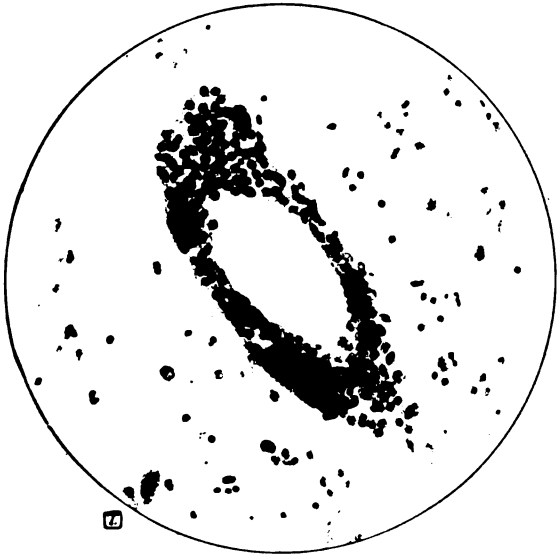


Fig. 48.—Transverse section of vessel in the brain in a case of sleeping sickness. (*From photo after Bettencourt.*)

lymph, increase and turbidity of cerebro-spinal fluid, are found. In all cases, as first pointed out by Mott, there is an extensive small-cell infiltration of the perivascular lymphatic tissue throughout the brain, cord, and meninges, varying in amount in different cases and in different anatomical regions. This, the essential pathological feature of sleeping sickness, recalls the very similar condition in general paralysis of the insane.

The nervous elements exhibit secondary degeneration changes.

Similar changes are described by Mott in the nervous system in dourine, and in chronic trypanosomiasis in the monkey. Mott has also pointed out that the lymphatic tissues throughout the body are similarly affected.

Digitized by Google

Diagnosis.—Chronic irregular fever, more especially if associated with enlarged cervical glands and, in the European, erythema multiforme, in a patient who has resided in tropical Africa at any time during the previous seven years, but more especially recently, suggests a tentative diagnosis of trypanosomiasis and detailed examination with this possibility in view. Diseases with which trypanosomiasis might be confounded are malaria, kala-azar, pellagra, syphilis, leprosy, and, in its later stages, beriberi.

Malaria, syphilis, and leprosy are easily excluded. As regards beriberi, there should be no difficulty if it be borne in mind that it is a disease of the peripheral, whilst trypanosomiasis is a disease of the central nervous system; that beriberi is non-febrile, and that trypanosomiasis is febrile. Kala-azar and trypanosomiasis, especially in their earlier stages, may be more difficult to differentiate; but the presence of enlarged glands, local œdema, and erythema multiforme in trypanosomiasis, and their absence in kala-azar, suffice for distinction. Blood or gland-lymph examination, or, if this be negative, hepatic or splenic puncture, should establish the diagnosis.

In pellagra the erythema is of a characteristic type. It is not ringed or fugitive as that of trypanosomiasis, and it affects principally the exposed parts of the body; the disease is of a much more chronic character, and, instead of lethargy, the mental condition, if implicated, is more that of insanity—melancholia alternating with mania and terminating in dementia. Further, in pellagra the symptoms are aggravated at particular seasons—spring and autumn.

General paralysis of the insane,* cerebral tumour, forms of meningitis, have features in common with trypanosomiasis and must be considered in diagnosis.

The microscopical diagnosis of trypanosomiasis is sometimes difficult. Anæmia as well as a large mononuclear leucocytosis occurs in trypanosomiasis. A wet blood preparation exhibits, even to the naked eye, a remarkable clumping of the red corpuscles. Held up to the light, such a preparation has a peculiar granular appearance, produced, as can be seen on microscopical examination, by agglomeration of the corpuscles into heaps and clusters, the usual rouleaux arrangement being absent. Such a disposition of corpuscles is significant of, though not peculiar to, trypanosoma infection. As a rule, the parasites in the peripheral circulation are few in number, many fields having to be hunted before a single example is discovered. Sometimes none can be found; rarely are they

* It has been stated that the serums of a proportion of cases of trypanosomiasis give a positive Wassermann reaction. More research on this subject is necessary.

Digitized by Google

abundant. In the same case they are sometimes present, sometimes absent. Centrifuging citrated blood may prove of considerable assistance. Dutton and Todd have emphasized the value of lymphatic-gland puncture and examination of the aspirated lymph, particularly in the earlier stages of the disease when the glands are soft and before they have become sclerosed ; then the trypanosomes are fairly abundant in the lymph. An ordinary hypodermic syringe suffices to aspirate a sufficiency of lymph. Films of the lymph so obtained are prepared and stained in the ordinary way. Cerebro-spinal fluid, obtained by lumbar puncture and centrifuged, affords another, though not always a practicable, means of finding the parasite. If the trypanosome is not found, information may be obtained from the lymphocytes, which are increased up to 100 per c.mm.. and from the amount of albumen which the cerebro-spinal fluid contains.

Failing discovery of the parasite by blood or lymph examination, recourse must be had to animal inoculation, 10 to 20 c.c. drawn from a vein being used for that purpose. Of the ordinary laboratory animals the most susceptible, and therefore reliable, are the guinea-pig, the rat, the dog, and certain monkeys—*Macacus* and *Cercopithecus*. Such inoculations are of value as a test of recovery, as well as for diagnosis.

It is probable that a complement-deviation test for human trypanosomiasis may be worked out on the same lines as the method described by Watson for *T. equiperdum* in dourine. In this case the antigen is prepared from the spleen of an artificially infected rat, ground up in 30 c.c. of normal saline and subsequently filtered.

The trypanosome is easily stained by most dyes ; convenient stains are those in use for malaria work. A $\frac{1}{6}$-in. objective suffices to find the parasite.

Treatment.—Although something may be done to relieve symptoms and delay the fatal issue in the sleeping-sickness stage of trypanosomiasis, it is only in the earlier stages of the infection and by the persistent and energetic use of arsenic or antimony, or both, that a cure can be effected, and that in a proportion of cases only. Other drugs have been shown to have some influence on the trypanosome infections of the lower animals, but their therapeutic value in those of man is practically negligible.

The effects of the administration of *arsenic compounds* on a heavily infected animal are very marked, after a preliminary and marked increase in the number of parasites in the peripheral circulation. According to Thomas, in from three to seven hours an adequate dose of atoxyl causes the trypanosomes to become swollen,

Digitized by Google

deformed, and almost motionless, their cytoplasm taking on a peculiar ground-glass appearance, becoming vacuolated, and presenting large dark granules. After seven or eight hours, coincidently with a marked increase of leucocytes—especially phagocytes—the parasites become rapidly fewer, and by the sixteenth or eighteenth hour completely disappear.

Arsenic, in the form of Fowler's solution or of orpiment, is sometimes given by the mouth; but this way of administering the drug, especially in Europeans, has been quite superseded by the intramuscular injection of a variety of relatively feebly toxic preparations, including atoxyl, soamin (sodium para-amino-phenyl-arsenoxide), arseno-phenylglycin, arsacetin, salvarsan,* etc.

Atoxyl, a meta-arsenic-anilin compound, introduced by Thomas, is probably the best of these, and the one most usually employed. Unfortunately it has one serious drawback—in large doses it is apt to give rise to optic neuritis, and consequent atrophy and blindness. The drug, therefore, must at once be stopped on the slightest threatening—dimness of vision or congestion of the disc—of such a calamity. Gastro-intestinal irritation and peripheral neuritis are also indications that it has to be suspended, at least temporarily, and the subsequent dose reduced.

Atoxyl is best given intramuscularly in 10-per-cent. solution in sterile normal saline. The solution should be freshly made and free from precipitate. The individual dose should not exceed 7 gr. The practice as regards dosage and the times and frequency of administration varies. Some advocate a 7-gr. dose once every fifth day until symptoms subside. After a few weeks, similar courses, lasting for a month and repeated at short intervals, are kept up for at least one year. Manson's practice was to give an injection of 3 gr. every third day, and to keep this up uninterruptedly for two years, unless symptoms of arsenical poisoning showed themselves, when the course was temporarily intermitted. Excellent results have been obtained from this method of giving atoxyl, both alone and in combination with tartar emetic by mouth or intravenously. Atoxyl has also been given intravenously in 10-gr. doses in 10 c.c. of normal saline weekly; but the risks of optic atrophy in doses larger than this are great. Daniels has been in the habit of prescribing antimony by the mouth, in the form of antiluetin, in ½- to 1-gr. doses, together with these drugs.

Antimony (tartar emetic) in the form of sodium tartrate hypo-

* Broden and Rodhain report good results on the Congo by intravenous injection of salvarsan; they insist that it is only of benefit in those cases where invasion of the spinal cord is negatived by microscopical examination of the spinal fluid.

Digitized by Google

dermically was shown by Plimmer and Thomson to have an effect upon *T. brucei*. In two cases of trypanosomiasis in man in which Manson used this drug intramuscularly the consequent local pain and irritation (culminating in tissue necrosis) were so excessive that in this form the treatment had to be abandoned. One of the patients, however, continued the drug by mouth to the extent of 1½ to 2 gr. daily, very highly diluted, a little being given in all his food and drink, and along with atoxyl injections, for over two years. He recovered.

The value of antimony in the treatment of trypanosomiasis is now so well established that, if possible, it should be employed in every case. It is far too irritating for intramuscular injection. The intravenous method is the one to be preferred, and as carried out now is free from risk. It is necessary to commence with ½ gr. dissolved in 10 c.c. of saline and injected directly into a vein; this dosage should be increased by ½ gr. on each occasion till a limit of 2 gr. as an individual dose is reached. It would seem advisable to give the injections on alternate days as in schistosomiasis (p. 566); should a small quantity of menstruum be used the resulting reaction is less severe. Most clinicians prefer the open method.

The solution must be slowly introduced, and great care taken that none of it escapes into the connective tissue surrounding the vein. Pain and swelling, and perhaps abscess, are apt to follow such an accident. With this in view it is well, before pouring the emetic solution into the receiver of the transfusing apparatus, to place in the latter an ounce or two of plain saline, and, when the emetic solution has nearly all run through, a similar quantity of saline.

Not infrequently during the progress of the transfusion the patient is seized with a fit of coughing, or with feelings of constriction of the chest and faintness. If these are severe they may be regarded as indications for stopping the flow of fluid. Usually, though not always, the transfusion is followed by smart fever, which soon subsides. A similar occurrence may follow intramuscular injection of atoxyl, and has been attributed to toxins liberated from the trypanosomes killed by the drug. Possibly the employment of organic compounds of antimony for intravenous injection may prove more suitable—forms which are less toxic to the human tissues and yet retain their specific action upon the parasites.

As with atoxyl, there are differences in the method of employing antimony injections. Some give them daily in courses of fifteen days at intervals of fifteen days; others, once a week; others, again, according to indications supplied by temperature and the microscopical examination of the blood. After the short fever

Digitized by Google

which may ensue, the administration of antimony is usually followed by marked relief of symptoms. As regards the total quantity to be given by this method, no rule can be laid down. Generally the amount of antimony totals well over 50 gr.

Unless contraindicated, atoxyl and antimony treatment should be combined or alternated. One or both should be instituted immediately the diagnosis of trypanosomiasis is established.

As pointed out by Ehrlich, certain strains of trypanosomes are "arsenic-fast," that is, they resist the action of the drug—a property which becomes hereditary and is continued in subinoculations into the lower animals. This undoubtedly accounts for the failure of arsenical treatment in a large proportion of cases. Presumably there are strains having a similar resisting power to antimony. As the atoxyl-fast trypanosomes may respond to antimony, and vice versa, both drugs should be employed in every case. In the face of so grave a disease great risks are justified.

In the treatment of trypanosomiasis, concurrently with the use of drugs, every effort should be made to keep the patient in good general health. Rest, warmth, and residence in a cool and healthy climate, the systematic use of quinine for any concurrent malarial infection, and the avoidance of fatigue and everything that might depress, should be insisted on.

The idea of cure must not be entertained until the patient has been free from all symptoms for many months, nor until the repeated injection of several cubic centimetres of his blood has failed to induce trypanosomiasis in susceptible animals.

Immunization.—Attempts have been made to procure a curative and immunizing serum, but, although a certain amount of success has attended these efforts in respect to the lower animals, as regards man they have failed.

Prophylaxis.—The indications for prophylaxis are based principally on the habits of *Glossina palpalis* and the existing conditions as regards the presence of the infection in a locality.

In endemic regions the fly areas should be located and avoided. If such regions have to be traversed, the journey should be made during dark nights, when tse-tse flies do not feed, or with such precautions as are used by the natives for the protection of their cattle in nagana-infected spots. Those who are compelled to live in tse-tse regions should have their houses and persons carefully guarded against the fly. Manifestly it is desirable—whether it is feasible is another question—to avoid localities in which the natives are affected, and to prevent the infection of the local tse-tse flies by surrounding people who have trypanosomes in their blood with

Digitized by Google

mosquito-netting; or by other measures, such as removing them from the usually very limited fly area to some neighbouring fly-free spot. Movements of infected individuals towards hitherto uninfected countries must necessarily be attended with great risk of the introduction of the disease. Whether such movements can be prevented in savage lands depends greatly on local circumstances. Wherever possible they should be prevented. Dutton and Todd suggest that an easily ascertained condition, more or less general in trypanosomiasis, namely, enlargement of the cervical glands, should be employed in eliminating dangerous individuals. Many years ago slave-dealers adopted such a method to shield themselves from loss. As a rough test it has some value. But in some cases of trypanosomiasis the glands are not appreciably enlarged at all times. Moreover, as they are often enlarged in other conditions, an injustice might be done in enforcing such a measure.

Hodges and his colleagues in Uganda inform us that the fly ground proper is always a very narrow strip indeed, not more than ten to fifteen yards, and always along the water's edge; and that the insects very rarely extend their feeding beat beyond sixty yards of this, whether on the land side or on the water side. It is true they may follow with great persistency a man who has just passed through this narrow belt, for several hundred yards, rarely as far as half a mile; but it is obvious that if the ten or fifteen yards at the water's edge be made unsuitable for the fly, as can readily be done by clearing it of jungle, there will soon be no flies to follow, and the place will become safe. Therefore, where feasible, fly spots, where there are landing-places, ferries, wells, or roads, should either be avoided altogether or be cleared of jungle for some yards—to be safe, thirty—from the water's edge. This is a practical measure of proved value in Uganda.*

Brilliant results have attended the efforts of the Portuguese to combat sleeping sickness in the island of Principe, where the annual mortality from the disease amounted to 83 per thousand of the population, and the local industry (cocoa) was threatened with extinction. In addition to jungle-clearing, drainage, blood examinations and segregation of infected, and destruction of possible animal reservoirs of the trypanosome, coolies, dressed in white and carrying on their backs a dark cloth smeared with birdlime, were sent into the jungle, and every night the flies caught were removed and counted. In three years 470,000 glossinæ were caught. As a

* Duke has found that if arseno-phenylglycin is injected into monkeys infected with trypanosomes, the presence of this drug in the bloodstream inhibits the subsequent development of the organism in the tse-tse fly.

Digitized by Google

consequence of this combination of sanitary measures the fly and the sleeping sickness were exterminated. Of course it was only the complete isolation and the limited size of the island that made such a result possible.

Koch, from observations in Uganda, suggested that trypanosomiasis may be communicated by the male during coitus. The phenomena of dourine and recent animal experiments support the idea, although the experiments referred to indicate that the risk is not great.

A complete scientific prophylaxis can be indicated with certainty only when we have full knowledge (1) of the habits of the tse-tse flies and of the reasons for their restriction to very limited and apparently capriciously distributed areas; (2) as to what vertebrates under natural conditions are normally hosts of *T. gambiense*. Experiment has shown that the glossina will bite any vertebrate, and that it can infect a large variety of mammals with the trypanosome. If this be the case in the laboratory it is reasonable to suppose that it is the case in nature also. Therefore, in the endemic regions of trypanosomiasis, the vertebrate fauna has to be reckoned with as a source and reservoir of infection.

In Uganda and elsewhere, principally with a view of preserving the hitherto uninfected from trypanosome infection, Government removed the entire population of the Sesse Islands and neighbouring shore of Lake Victoria Nyanza to fly-free areas in the interior. It was hoped that, the human source of trypanosome supply being thus denied them, the tse-tse flies would cease to be infective. Unfortunately, this hope has been disappointed. Three years after depopulation of the districts involved, Bruce ascertained that the local flies could still convey the disease to laboratory animals. Manifestly, *T. gambiense* can flourish under natural conditions in vertebrates other than man. The large game is now regarded as a probable reservoir for *T. gambiense*, as it is known to be for the *T. brucei* of nagana.

The introduction of *T. gambiense* into other countries is a grave possibility. It is true that it must have been frequently introduced into America in the days of slave importation and that it did not spread there; but as regards India and other Asiatic countries, which hitherto have had little or no communication with the West Coast of Africa, no introduction on a large scale has occurred, and we have no assurance that, if introduced, the parasite would not find some appropriate transmitter. According to some authorities, nagana and surra are the same disease; if so, the causal trypanosome can be transmitted by blood-sucking flies other than the tse-tse.

Digitized by Google

What holds good for *T. evansi* and *T. brucei* might equally apply to *T. gambiense*. Furthermore, the possibility of the introduction of the fly host of the trypanosome of sleeping sickness, *G. palpalis*, into other tropical countries must not be lost sight of.

TRYPANOSOMA RHODESIENSE

The discovery by Stephens and Fantham that the trypanosome found in sleeping-sickness cases originating in Nyasaland, Tanganyika Territory, Rhodesia, and Portuguese East Africa presents certain peculiarities when passed through the rat, that it was associated with a highly virulent and resistant form of the disease, that animals immunized against *T. gambiense* succumbed to the

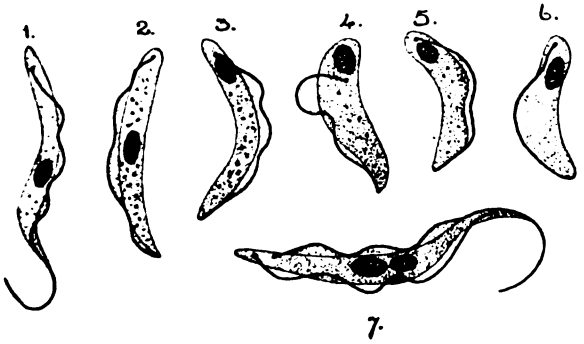


Fig. 49.—Trypanosoma rhodesiense. (*After Laveran.*)

1 and 2, Normal forms in blood of man; 3–6, various stages of posterior displacement of the nucleus; 7, a dividing form.

Rhodesian trypanosome, and especially, as proved by Kinghorn and Yorke, that it was transmitted by *Glossina morsitans*, justifies the conclusion that, if not a distinct species, *Trypanosoma rhodesiense*, as it has been named, is a very definite variety, and that in practice it must be regarded as such.

Since *Glossina palpalis* has been found in Rhodesia in one place only, on Lake Mweru, and not at all in Nyasaland, it is possible that its rôle as regards this trypanosome has been taken by *Glossina morsitans*.

In human blood (Fig. 49, 1, 2), *T. rhodesiense* is morphologically indistinguishable from *T. gambiense*; but if it is passed through the rat a small but variable proportion of the parasites, especially the stumpy forms, will be seen to have their nuclei located posteriorly to the kinetonucleus, that is to say, at the nonflagellar end of the organism. It also, as occasionally in man, exhibits a marked

Digitized by Google

periodicity, disappearing from the bloodstream for weeks at a time.

According to Kinghorn and Yorke, the peculiarities in the range, distribution, and fly intermediary of *T. rhodesiense* receive their explanation in the circumstance that the developmental cycle is dependent on atmospheric temperature. High temperatures (75°–85° F.) favour development in the fly, low temperatures (60°–70° F.) are against it. These same observers consider the large game of the country to be a reservoir of the parasite.

Later experiments by Bruce and his co-workers have shown that *T. brucei*, when injected into rats, exhibits the same proportion of posterior-nucleated forms as *T. rhodesiense*. From this and other facts these observers suggest that *T. rhodesiense* is none other than *T. brucei*, that 37 per cent. of the wild game in the fly-country harbour pathogenic trypanosomes, and that the waterbuck, hartebeest, reedbuck, and duikerbuck are a source of danger to man.

Taute, who has carried out much research work on this important subject in Portuguese Nyasaland, does not agree in all respects with the views of Kinghorn, Yorke, and Bruce. He points out that the trypanosomes in naturally infected game or domestic animals can be regarded as a potential cause of sleeping sickness only if they are actually shown to be pathogenic to man; and he maintains that the wild game and domestic animals do not play any part in the spread of sleeping sickness, at all events in the sense of Kinghorn and Yorke. Merely to infect laboratory animals with a trypanosome morphologically identical with *T. rhodesiense* does not prove that this trypanosome is *T. rhodesiense*, or that the district from which the trypanosome came is a sleeping-sickness area. He says that in East Nyasaland *T. brucei* can be distinguished from the trypanosome of sleeping sickness only and solely by the fact of its non-pathogenicity to man. Taute supports these views by some very significant experiments. *G. morsitans* fed on animals infected with *T. brucei* were subsequently fed to two men; the result was negative, though a number of control animals fed simultaneously died. Taute injected himself with 2 c.c. of blood from a trypanosome-infected dog, the trypanosomes being of the Rhodesian type; there was no bad effect. Fourteen days later he injected 90 c.c. of his own blood into susceptible animals; these animals did not become infected—showing that the human organism has the power to kill this particular trypanosome. More recently, the same investigator has pointed out that the natural incidence of the disease is against the identity of the two parasites (*T. brucei* and *T. rhodesiense*). Sleeping sickness of the *rhodesiense* type occurs in

Digitized by Google

Rhodesia, Nyasaland, and the Rovuma district in relatively small circumscribed foci, whereas *T. brucei* is uniformly spread over very large extents of territory ; in heavily infected nagana districts Taute examined the blood of 1,500 children for trypanosomes with a negative result. During the war in East Africa he injected himself a second time with 5 c.c. of mule blood containing posterior-nucleated forms of trypanosomes, as well as 129 negroes accompanying the expedition, without any symptoms supervening or the appearance of trypanosomes in the bloodstream. The result of these experiments, he claims, definitely disproves that *T. brucei* is in any way pathogenic to man.

Symptoms are similar to those evoked by *T. gambiense*, though febrile paroxysms are more frequent and severe glandular enlargement is not frequently met with. The disease generally runs a much more rapid course.

Treatment.—Atoxyl and antimony tartrate, generally so potent in *T. gambiense* infection, seem to be relatively powerless in *T. rhodesiense* cases, unless they are taken in hand very early. Daniels and Newham have reported favourably upon a method of treatment by intramuscular injections of 30 min. of Martindale's injectio antimonii oxidi, given twice daily. These injections, they say, are painless and cause no necrosis. Up to date there is but one record by the same investigators of the survival of a European infected with *T. rhodesiense ;* this case received over 500 gr. intravenous antimony tartrate, in 2½-gr. weekly doses, spread over a period of two years.

Prophylaxis.—Prompted by the results of his investigations that the big game act as a reservoir for *T. rhodesiense*, Yorke has advocated the extermination of this interesting fauna. Seeing that this terrible disease is thought to be spreading, that it has already crossed the Zambesi, that the range of *G. morsitans* extends as far south as Zululand, and that it is in great measure dependent on these animals, the destruction or driving back of the wild game in *G. morsitans* countries seemed to be the only practical measure. Now, fortunately, as a result of Taute's work, these drastic measures would appear to be not so necessary, for it is possible that the game only act as a carrier of *T. rhodesiense* in certain circumstances. The ideal to be aimed at is the extermination of *Glossina morsitans* in sleeping-sickness areas, and this will be effected with the cultivation and development of the country. A system of afforestation seems to hold out the most immediate prospects of success in any preventive measures undertaken. It has been ascertained that certain species of hymenopterous flies are parasitic on glossina

Digitized by Google

pupæ as *Mutilla glossinæ*, but, at the most, these can only restrict the distribution of *G. morsitans* in a very limited degree.

Trypanosoma cruzi (Schizotrypanum cruzi)

Synonyms. — American Trypanosomiasis; Derrengadera; Chagas' Disease.

History.—Chagas has shown that a form of trypanosomiasis, especially common in children, is endemic in parts of the state of Minas Geraes in Brazil, and that it is transmitted to man and the domestic animals by a species of bug, *Conorhinus megistus* (formerly considered to belong to the genus *Lamus* or *Triatoma*). Allied species and certain other biting insects appear to have the power of transmitting the infection, at all events under experimental conditions. In Venezuela the intermediary host is probably *Rhodnius prolixus*. The natural reservoir is supposed to be the armadillo, of which 50 per cent. are infected with this trypanosome. A recent communication by Escomel reports the discovery of a human trypanosome in Peru; this Yorke considers to be specifically distinct, and he has suggested the name *Trypanosoma escomeli*.

Geographical distribution.—Originally thought to be confined to Brazil, the disease is shown by recent researches to occur also in Venezuela (Tejera). Whether it is found in Peru or not is still undecided.

Symptoms.—The disease assumes a variety of aspects according to the organs more particularly affected by the parasite, individual susceptibility, and the occurrence of reinfection. It is frequently fatal, and in those who recover is apt to entail conditions, physical and mental, resembling cretinism.

Chagas recognizes acute and chronic types. In the former, shortly (ten or more days) after the bite of the transmitting insect, which is painful, high fever supervenes together with enlargement of the thyroid gland, lymphatic glands (especially the cervical), spleen, and liver, myxœdematous swelling of the face, and transient œdemas in different parts of the body. There may be indications of meningo-encephalitis. These symptoms come and go during a variable period, and terminate either in death or in recovery, or in the chronic form lasting for years.

In the chronic form there is well-marked enlargement of the thyroid,* with accompanying myxœdematous symptoms, as loss of

* Rabbits and guinea-pigs infected with *T. cruzi* show no changes in the thyroid gland; it is therefore contended by Langhans and Wegelin that this special form of goitre described by Chagas is probably an endemic goitre complicated by a superimposed trypanosome infection.

Digitized by Google

hair, mental debility, etc. The lymphatic glands are always enlarged. In some instances there is marked bronzing of the skin, as in Addison's disease, depending on implication of the suprarenal capsules. In others, where the brunt of the infection has fallen on the heart, there is great irregularity in the action of this organ. In yet others aphasia, ataxia, spasm, athetosis, tremor, or other nervous symptoms indicate that brain, or spinal cord, or both have become implicated. Generally there is a combination of several of these conditions. Throughout, an irregular fever comes and goes, and there is always pronounced anæmia.

The chronic form is that most commonly encountered in youths or adults; it is probably carried on from infancy or childhood, or kept up by reinfection.

The parasite.—During the febrile attacks the parasite (Fig. 50) in variable numbers is to be found in the blood, free or, rarely, partially included in red blood-corpuscles (Chagas). It averages about 20 μ in length and has the usual trypanosome characters. The undulating membrane is narrow and the nucleus and kinetonucleus are large. It is easily cultivated.

After ingestion by the insect intermediary the trypanosomes multiply in the gut. Some pass out with the fæces, which thus become infective if inoculated into a wound, or if applied to a mucous surface as the conjunctival sac (Brumpt). This, however, is not the normal way in which the infection is conveyed to man. In the midgut of the conorhinus, crithidial forms and, at a later stage, minute trypanosome forms develop. It is the latter that, passing into the salivary glands, become the agents by which the infection is established. Eight days elapse after feeding on infected blood before the bug itself becomes infective.

Brumpt has observed a similar development of the parasite in other species of Conorhinus, *C. geniculata*, *C. infestans*, *C. sordida*, *C. vitticeps*, *C. dimidiata*, *C. sanguisuga*, and other hemiptera, *Cimex lectularius* and *C. boueti*, *Rhodnius prolixus*, as well as in the ticks *Ornithodoros moubata* and *Rhipicephalus sanguineus*. In view of the ubiquity and vast geographical range of these possible vectors, the question arises why the spread of Chagas' disease is relatively so restricted.

Arrived in the human body the parasite multiplies, not in the blood (dividing forms are never found there), but in the cells of various organs, including the striped muscular fibres, especially of the heart (Fig. 51), vertebral muscles, and lower extremities; also in the bone-marrow, the thyroid gland, suprarenal capsules, nerve fibres and cells, testes, connective tissue, and various other organs.

Digitized by Google

In these it assumes a leishmania form (Fig. 50, 7, 8), divides and subdivides, distending the including cell till this becomes a mere cyst in which the parasites revert to the trypanosome form. The cyst then bursts and the trypanosomes escape into the tissues, ultimately

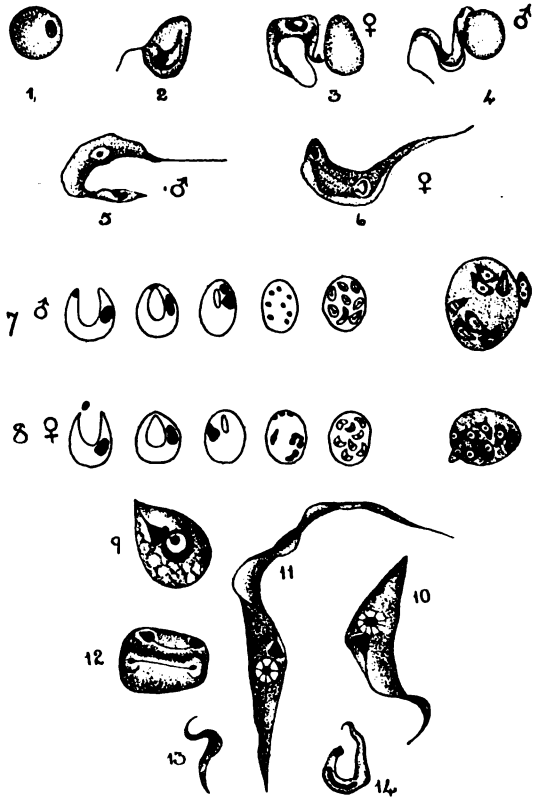


Fig. 50.—Trypanosoma cruzi. (*After Chagas.*)

Figs. 1–6.—*Forms in human blood:*
1, 2, Supposed endocorpuscular forms; 3, 4, trypanosomes adhering to red cells 5, 6, so-called male and female forms.
7 and 8.—*Schizogony in the endothelial cells of pulmonary vessels in man:*
(Diagrammatic representation of the pulmonary cycle, cyst formation, and liberation of young trypanosomes. It is doubtful whether ♂ and ♀ cycles as described by Chagas really exist. *See* p. 141.)
9–14.—*Forms found in Conorhinus megistus:*
9 and 10.—Forms from midgut showing development of flagellum; 10 and 11, forms from the hindgut; 12, simultaneous division of nucleus and centrosome; 13 and 14, forms from salivary gland, under a lower magnification.

finding their way into the blood concurrently with an attack of fever. This is the form of schizogony by which the infection is kept up in the individual.

Digitized by Google

According to Chagas the gamete providing for the exogenous cycle in the insect arises from certain trypanosomes which, lodging in the lungs, lose their flagella and, approximating their extremities, form a ring, and then a sphere in which the nucleus divides, giving rise to eight daughter-spheres. These elongate and, escaping, enter the red blood-corpuscles and become male and female trypanosomes, thus providing for the exogenous cycle in the insect (Fig. 50). Later work, however, has thrown doubts upon this cycle, as provisionally outlined by Chagas.

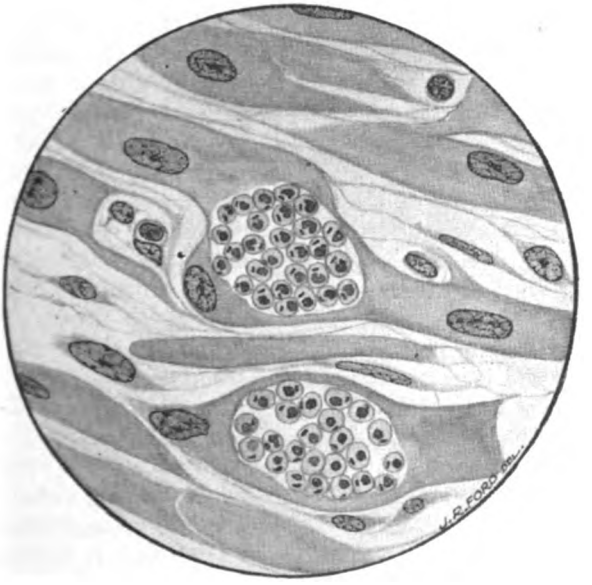


Fig. 51.—Trypanosoma cruzi: schizogony in heart-muscle.
(*After J. Gordon Thomson.*)

In the insect the parasite is not transmitted hereditarily, but the nymph, as well as the mature conorhinus, is capable of ingesting and transmitting the parasite. In the endemic districts all the bugs and many domestic animals are infected. Chagas considers that the armadillo, whose burrows are haunts of the conorhinus, is the normal host of the parasite and a principal reservoir for the infection. Maggio and Rosenbusch have drawn attention to the fact that, although a bug (*Conorhinus infestans*) is widespread in the Argentine, yet Chagas' disease is unknown in that country, and at the same time the intestinal contents of this insect contain developmental trypanosomes, which, when injected into guinea-

Digitized by Google

pigs, undergo development in the muscular tissue. An explanation of this interesting observation is not yet forthcoming.

Pathological anatomy.—Inflammatory and consequent degenerative changes, the result of the presence of the parasite, are in evidence in most of the affected organs. Under the microscope the cyst-like distended cells containing the parasite are to be found, particularly in the striated muscular fibres, and especially in those of the heart. The thyroid is enlarged, often sclerosed, with cystic cavities containing colloid material. The lymphatic glands and the spleen are also enlarged, the liver is fatty, serous effusions in pleura and peritoneum are common, and there may be evidences of meningo-encephalitis with infiltration about the vessels.

Diagnosis.—The trypanosome is usually present in very small numbers, and may require prolonged search for its detection. A guinea-pig may be inoculated with the patient's blood, and the parasite be subsequently discovered in the bloodstream, or the developmental forms in the muscles of that animal.

Brumpt has suggested that, in the absence of visible parasites in the blood, developmental forms may be demonstrated in the alimentary tract of conorhinus larvæ which have been fed on these patients.

Prophylaxis.—This should be directed principally to the suppression of the insect concerned—*Conorhinus megistus* (Plate IX.). It is a large black insect belonging to the family Reduviidæ, with numerous symmetrically arranged red markings; it is well known to the natives, who call it "barbeiro." The nymphs bite and can convey the infection, but the adults, having wings, are more dangerous. In the daytime they live in the grass walls and roofs of the dirty native houses, coming out after dark in search of their food—blood. Their habits indicate better and cleanlier housing, sleeping off the ground, and protection by mosquito-netting.

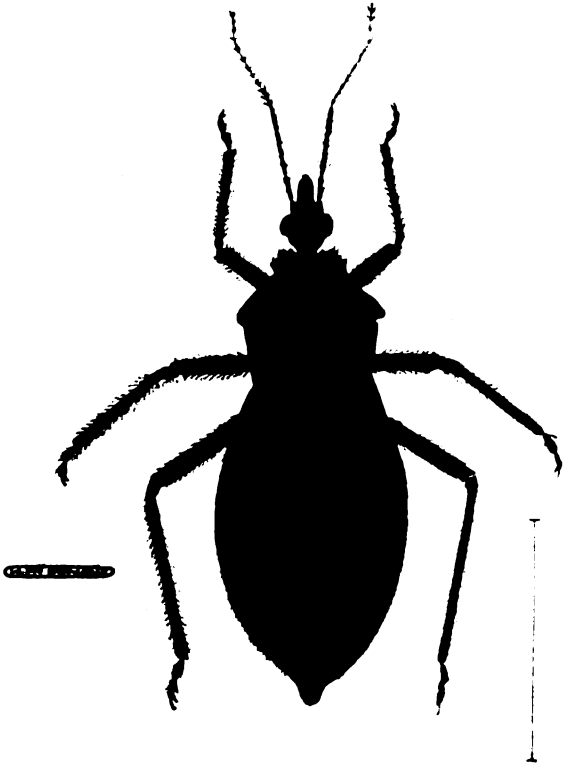
Bugs of this genus have a wide distribution in the southern United States and South America. One species, *Conorhinus protractus*, lives in the nests of a wood-rat and attacks man in California and Arizona, so that the subject of prophylaxis of this disease is likely to engage the serious attention of sanitarians in the future.

Treatment.—We know of no specific remedy. Arsenicals and antimony have failed in experimental animals. Treatment, therefore, must be on general lines.

Other Forms of Trypanosomiasis in Man

Seeing that most of the trypanosomes hitherto studied experimentally are capable of living in a variety of vertebrate hosts, it

Digitized by Google



CONORHINUS MEGISTUS. (*After Chagas.*)

PLATE IX.

Digitized by Google

Digitized by Google

seems probable that other members of this group of parasites, in addition to *T. gambiense*, *T. rhodesiense*, and *T. cruzi*, may find in man at times a suitable host. Apparently *T. lewisi*, *T. evansi*, and *T. vivax* do not thrive in man, but that circumstance does not warrant the inference that he is completely immune against these and all other species. For instance, Macfie has recently reported a mild form of trypanosomiasis in man in which the parasite was morphologically similar to *T. vivax*.

As the subject of trypanosomiasis in man is one of great and growing importance in tropical pathology, it is desirable that the student should have some practical acquaintance with the appearance and diagnosis of this type of parasite before he is called upon to deal with it in actual practice. A table of pathogenic trypanosomes compiled by Bruce, which summarizes the present knowledge on this subject, is therefore given in Appendix I., at p. 758, together with further details. It must be remembered that any attempt at classification is merely tentative, and the one given is based upon three points—morphology, location of development of infective forms in the tse-tse fly, and their action upon animals.

The Tse-tse Flies (Plate X.)

(Genus *Glossina*, Wiedemann, 1830)

The species forming the genus *Glossina* are sombre-coloured, narrow-bodied flies from about 6 or 8 to 13·5 mm. long, with a thick proboscis (i.e. proboscis enclosed by the palpi) projecting horizontally in front of the head. Their wings are large, of a brownish hue, and present a characteristic venation (Plate X.) somewhat resembling that of the warble-fly (*Hypoderma*). The most striking peculiarity in the wing is the course of the fourth longitudinal vein, which about the middle of the wing bends abruptly upwards to meet the short and very oblique anterior transverse vein; here describing a right angle, it runs obliquely downwards to meet the posterior transverse vein, and then turns upwards to reach the margin of the wing well in front of the apex.

When a tse-tse is at rest its wings overlap on the back, closing over each other like the blades of a pair of scissors (Fig. 52). This resting attitude of the wings, besides giving the fly a peculiar elongated appearance, renders it readily distinguishable from other blood-sucking diptera with which it might be confounded, e.g. the stable-fly (*Stomoxys*) and the cleg (*Hæmatopota*).

Stomoxys is smaller in size, has short palpi not protecting the proboscis, and its wings diverge at an angle when resting. *Hæmatopota* presents prominent antennæ and its wings are tectiform when closed, i.e. they meet together at the base like the roof of a house and diverge slightly at the tips.

In some species of Glossina the abdomen is crossed by sharply defined dark-brown bands, interrupted at the middle line. In the males, beneath the end of the abdomen the external genitalia form a conspicuous knob-like protuberance which renders the sexes easily distinguishable.

Digitized by Google

In Glossina the palpi are long, deeply grooved on their inner sides, and closely applied to the proboscis, which they almost entirely conceal when it is not in use, the only uncovered portion being a peculiar large bulb-like expansion at the base. The proboscis consists of three parts (Fig. 52), *labrum*, *hypopharynx*, and *labium*.

The genus *Glossina* belongs to the sub-family STOMOXYDINÆ, of the family MUSCIDÆ. The nearest related genera are *Stomoxys*, *Lyperosia*, and

Fig. 52.
Tse-tse fly at rest.

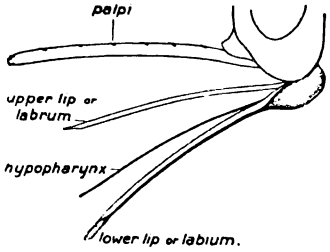


Fig. 53.
Mouth-parts of glossina.

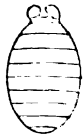


Fig. 54.
Pupa stage of glossina.

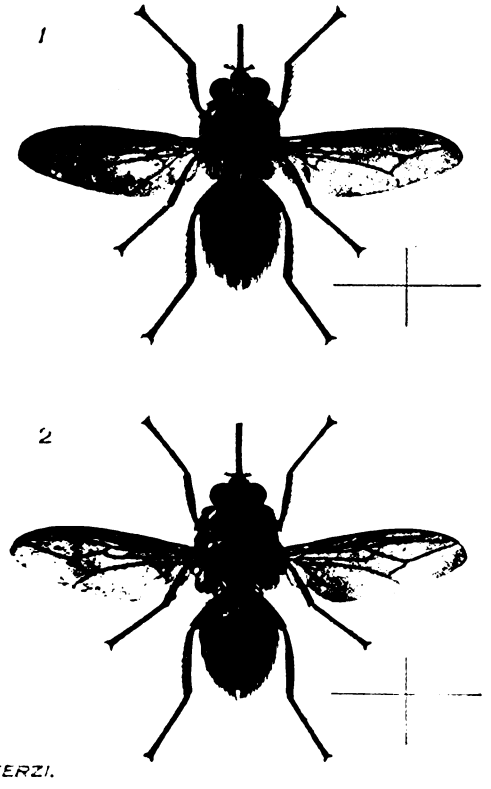
Hæmatobia; but on account of its limitation to the Ethiopian region, its peculiar structural features (bulb at the base of proboscis, remarkable male genitalia, characteristic venation of wings), and its aberrant mode of reproduction, *Glossina* presents a marked individuality.*

The genus at present comprises seventeen species, though this number must not be considered final, as new species are discovered from time to time. Austen arranges the genus into four groups. (*See* Table following p. 146.)

Distribution.—Tse-tse flies are confined to Africa and the south-western corner of Arabia. Some species, such as *G. fusca* and *G. morsitans*, have a very wide range throughout the greater part of intertropical Africa. *G. palpalis* is also widely distributed, ranging from the Senegal to Angola on the west, and throughout the Lualaba-Congo system to the Victoria Nyanza, Tanganyika, and Upper Nile at least as far north as Mvolo in the Soudan. The range of *G. austeni*, an East African species, extends from Jubaland to Zululand. *Glossina morsitans* ranges southwards to Bechuanaland, North-Eastern Transvaal, and Zululand, and northwards to Senegambia, Southern Kordofan, and Southern Abyssinia. *G. longipalpis* ranges through West Africa as far north-west as Senegal and south-east to the Katanga district of the Belgian Congo. *G. pallidipes* is found throughout East Africa from Zululand to the northern boundary of British East Africa, while westward its range extends to the Katanga district of Belgian Congo. Other species appear to be more restricted. *G. longipennis* is found in Somaliland and adjacent regions; *G. tachinoides* has a wide range in West Africa, and also occurs in Southern Arabia; *G. pallicera* ranges from Sierra Leone to Belgian Congo;

* Prof. Newstead in 1911 introduced a classification of species of *Glossina* based on a study of the male genitalia, which in this genus are characteristic. If macerated in potash the hypopygium can be turned backwards so as to display various complicated structures, namely, the superior claspers, the editum, the inferior claspers, the harpes, the juxta or penis sheath, the median process, and the connecting membrane. All these vary in shape in different groups; the median process and connecting membrane are found only in some of them.

Digitized by Google



1, Glossina palpalis. 2, G. morsitans.

TSE-TSE FLIES.

PLATE X.

Digitized by Google

Digitized by Google

G. fusca ranges from Sierra Leone to Uganda; *G. brevipalpis* is common in South-Central and East Africa; *G. caliginea* is found in Southern Nigeria. Knowledge of their topographical distribution is an important matter. The species of *Glossina* are never found on mountains; they are seldom seen above 3,000 feet; they are absent from extensive plains or other open places; they are rarely met with in close cultivation. Cover in the nature of bush, trees, or forest is essential, and the species of the *G. palpalis* group are restricted to the neighbourhood of water, being found along the banks of rivers, brooks, and springs, round the coasts of lakes, and on slow rivers and lacustrine islands. They do not usually frequent a sudd-covered or sedgy-banked river or lake shore or sedgy swamp, unless continuous with a belt of trees. The members of the *G. morsitans* group, however, as well as certain other species such as *G. brevipalpis*, are far from being confined to the immediate vicinity of water. The tracts infested by tse-tse flies vary greatly in disposition and extent according to the species concerned and the local or seasonal conditions. Thus, a so-called "fly belt" or "fly area" may be represented in one case by a narrow border of forest, but a few yards in width, along the edge of a stream; in another by a patch of "orchard bush;" or yet again, as sometimes in the case of *G. morsitans* or *G. brevipalpis*, by a wide expanse of bush-covered or wooded country extending for many miles. It frequently happens that "fly belts" undergo enlargement during the rains and a corresponding shrinkage during the dry season, the flies extending their area of occupation in the period of maximum cover, and withdrawing again to the shelter of thicker patches of bush, or true forest, when bush fires or the withering of foliage threaten their exposure to the fierce heat of the sun.

Reproduction.—The species of *Glossina* do not lay eggs as do the majority of the Diptera, but, as in the case of forest-flies (*Hippoboscidæ*), the eggs hatch, and the larvæ feed, develop, and moult within the body of the parent, so that when extruded they are practically ready to pupate. In fact, the extruded larva becomes a pupa (Fig. 54) within an hour or two, the larval skin becoming a dark, rigid puparium. When extruded, the fully-grown larva is nearly as large as the abdomen of the mother; it is a yellowish ovoid body composed of twelve segments and presenting two small hooks at the anterior pole, and two respiratory protuberances at the posterior extremity, which is black. A female tse-tse fly deposits her larvæ singly, at intervals of about a fortnight or three weeks, invariably choosing as a nursery a shaded spot where cover for the pupating larva is available in the form of loose, dry sand, humus, or vegetable débris. The necessary facilities in this respect are frequently afforded by the ground beneath fallen trees, where tse-tse pupæ or empty pupa-cases are sometimes found in considerable numbers. The perfect insect emerges from its pupa-case in about four to nine weeks.

Habits.—All tse-tse flies feed on blood, certain species, such as *G. morsitans*, exhibiting great persistency and voracity in their attacks on man and animals. The blood-sucking habit, contrary to what is the case among horse-flies (*Tabanidæ*), *Simuliidæ*, and mosquitoes (*Culicidæ*), is not confined to the females, but is common to both sexes. *G. palpalis*, like *G. morsitans*, is active and ready to attack throughout the day, from an hour or so after sunrise onwards. As a general rule, *G. brevipalpis*, *G. fusca*, and *G. pallidipes*, all three of which haunt by preference the edges of paths, spend the greater part of the day resting motionless on tree-trunks. Though sometimes aggressive in the early morning, *G. brevipalpis* does not usually leave its hiding-places until late in the afternoon, when it remains on the wing until about half an

Digitized by Google

hour after sunset. *G. fusca*, a more bloodthirsty species than *G. brevipalpis*, flies more silently, and as a rule bites only after dark. The period of activity of *G. pallidipes*, on the other hand, is usually in the afternoon, commencing somewhat earlier than and terminating before that of *G. brevipalpis*.

While *Trypanosoma gambiense* and *T. rhodesiense* are conveyed respectively by *G. palpalis*, *G. morsitans*, and possibly *G. tachinoides*, the rôle, if any, of the other species of *Glossina* in the dissemination of human trypanosomiasis is as yet unknown.

A synopsis of the characters of the four Glossina groups follows.

Digitized by Google

CHAPTER VIII

LEISHMANIASIS

UNDER the term Leishmaniasis at least three diseases of man are included—

1. KALA-AZAR.
2. ORIENTAL SORE.
3. ESPUNDIA.

These diseases, though clinically quite distinct and having each a definite topical and geographical distribution, are all associated with what optically appears to be the same organism, *Leishmania*. But though their respective organisms appear to be morphologically identical, it is by no means justifiable to conclude that they are specifically identical. The Leishmania form is common to many protozoa; it is merely a stage—an immature stage—and until the life-history is quite complete, and the natural history of the respective parasites of these diseases has been worked out, our judgment as to their identity or otherwise should be suspended. If it turn out to be the case that the germ causes of the various clinical forms of leishmaniasis are specifically identical, we shall have to conclude that the special pathogenic properties of these germs have been conferred on them during their extracorporeal life, especially by passage through particular animal intermediaries. Herein lies a wide field for future investigation.

1. KALA-AZAR

Synonyms.—Tropical Splenomegaly; Black Sickness; Sirkari Disease; Sahib's Disease; Burdwan Fever; Kaladunkh; Dum-dum Fever; Ponos.

Definition.—An infective disease characterized by chronicity, irregular fever, enlargement of the spleen and often of the liver, the presence in these and other organs of *Leishmania donovani*, emaciation, anæmia, leucopenia and relative increase of large mononuclear leucocytes, frequently a peculiar hyperpigmentation of the skin, and a high mortality.

History.—The earliest description of this disease is by Clarke (1882), who stated that as far back as 1869 the attention of administrative officers in Assam had been directed to a peculiar

Digitized by Google

disease called by the natives kala-azar, the ravages of which decimated, and in some instances almost depopulated, numerous districts in the Garo Hills. Notwithstanding its peculiar clinical features, its great fatality, its mode of spread along the lines of communication, the almost constant absence of malaria parasites from the blood, and the inefficacy of quinine treatment, until comparatively recently kala-azar was regarded by the majority of physicians as "a bad form of malaria."

In 1889 Giles, who had been appointed to investigate the etiology of kala-azar, denied its malarial nature, and stated that the disease was "neither more nor less than ankylostomiasis." In 1896 Leonard Rogers and in 1898 Ronald Ross were appointed to re-investigate the disease; both considered it a severe form of malaria.

Owing to the absence of malaria parasites, the inefficacy of quinine, and the absence of tertian or quartan periodicity in the cases of tropical splenomegaly Manson had studied in England, he had come to regard this disease as non-malarial and as one *sui generis*, and suggested in 1903 that the disease might be a trypanosome disease.

A few months later Leishman wrote that in 1900 he had discovered certain small oval bodies in the spleen-pulp of a soldier who had died of dum-dum fever at Netley, and that he surmised these bodies to represent degenerative forms of a trypanosome. In July, 1903, Donovan in India corroborated Leishman's discovery, and it then transpired that Marchand earlier in the same year had found similar bodies in a patient from China.

In December, 1903, Manson found similar bodies in the spleen of a patient from India suffering from the same disease, and was able to show that these bodies were not endocorpuscular parasites.

Geographical distribution.—From observations by a number of investigators we now know that kala-azar is a widely distributed disease. It is found in various parts of the eastern side of India, in China, Arabia, the Sudan, Central Africa, Tunis, Sicily, Italy, Algeria, Crete, Spain, Portugal, Greece and the Grecian Archipelago (where the disease known as "ponos" was proved by Gabbi to be infantile kala-azar), Malta, the Caucasus, Turkestan, Central and South America, South Africa, etc. Amongst the most important contributions to the literature of the subject are those of Christophers, who showed that the parasite attacks the endothelial cells; of Leonard Rogers, who in cultivating the parasite obtained a characteristic flagellated form; of J. H. Wright of Boston, who found parasites morphologically indistinguishable from those of

Digitized by Google

kala-azar in the granulation cells of tropical sore; of Nicolle and Comte on the occurrence of the same or a similar parasite in children and dogs in Tunis, and in kittens in Algiers; * of Laveran on experimental leishmania.

Epidemiology.—Our knowledge of the epidemiology of kala-azar is gathered mainly from the Assam epidemic, which began about 1870, when the disease appears to have been introduced from Rangpur. Rogers believed it was originally introduced from Bengal, a theory supported by the names of "Sirkari disease" and "Sahib's disease" given by the Garos, who state that it was unknown among them until after the English took over their country. The epidemic advanced slowly along the valley of the Brahmaputra, taking seven years to spread less than a hundred miles. The introduction of the infection into a village was almost invariably traced to someone coming with the disease on him from an infected locality, though some isolated localities escaped in a remarkable manner. Generally it clung to a place for about six years, and then disappeared without any apparent change in the local conditions. A house seemed to retain the infection for many months; the natives considered that it could not be reoccupied with safety under one year. During the course of the epidemic kala-azar never extended far above the level of the Brahmaputra valley, the disease appearing first at the foot of the hills, and then spreading between them along the patches of low, flat, terai country.

On account of its deadliness, kala-azar as it swept onwards became a terror to the natives. Those suffering from the disease were turned out of the villages; sometimes they were made unconscious with drink, taken into the jungle, and burnt to death. Some villages cut off all communication with neighbouring villages for fear of infection; other villagers deserted their homes and even migrated to a different district.

Although the foregoing is the only recorded example of kala-azar as a widespread and active epidemic, it had been recognized that a disease clinically identical occurred sporadically in several places in India, the Sudan, China, and South America. Apparently, then, kala-azar occurs both as a sporadic and as an epidemic disease. In 1904 leishmaniasis was discovered in Tunis by Cathoire, and important studies by the Sergents, Nicolle, and many others have shown that the parasite occurs in many of the islands and

* Nicolle gave the name *Leishmania infantum* to this variety of the parasite in order to call attention to the special liability of children to the infection in Mediterranean countries, and not because he considered it specifically distinct from the Indian form, which attacks adults and children indifferently.

Digitized by Google

countries in the Mediterranean basin; that there it is practically confined to young children—infantile kala-azar—*Leishmania infantum;* and, further, that whilst in India dogs are rarely affected, in the Mediterranean basin a large proportion of these animals are naturally the subjects of leishmaniasis.

Etiology.—The kala-azar parasite (Plate XI., Figs. 1–4) has now been relegated to the genus *Leishmania.* We know two stages of this body, intracorporeal and extracorporeal. Possibly these represent respectively asexual and sexual forms; the former found only in man and in some other vertebrates, the latter obtained in artificial culture media and, it may be, in certain insects—flies, bugs, fleas, lice, mosquitoes.

The distribution of the parasite within the body of man is very general. Apparently its special habitat is the endothelial cells of blood-vessels and lymphatics. It is particularly abundant in the spleen (Fig. 55), in the liver, and in the bone-marrow; but it also occurs in the lung, in the kidney, in the mesenteric and other

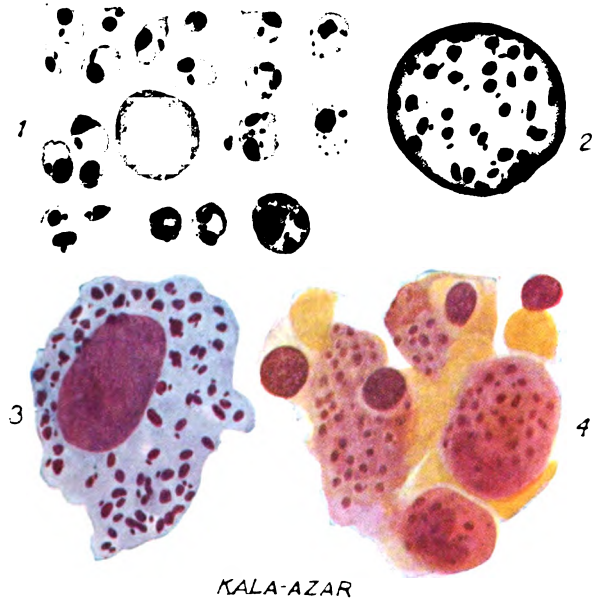
Fig. 55.—Kala-azar parasites from the spleen, stained.

lymphatic glands, in petechiæ, in the arachnoid, in ulcers involving the intestinal mucosa, and in papules and ulcers of the skin. It occurs also in the blood, though generally in very small numbers, being found there both in polymorphonuclear and mononuclear leucocytes, but very rarely in the red corpuscles.* In the blood it is in greatest abundance towards the termination of the case, especially during fever, and when intestinal symptoms are present (Donovan).

The Leishman-Donovan body, as it is generally called, is a small ovoid or roundish organism measuring from 2 to 4 μ in diameter. When stained according to Leishman's method it shows two lilac-coloured chromatin masses, one larger than the other, enclosed in a cytoplasm having a faint bluish tint about the periphery. The larger chromatin mass is the trophonucleus, which may be oval and centrally placed (resting stage), or elongated and at the periphery (predivision stage). The smaller chromatin mass is the blepharoplast; it is usually in the shape of a short rod, and is

* When existing in the blood in small numbers their presence can, in the hands of experts, be demonstrated by the N.N.N. cultural method. Centrifugation of the blood is of little use.

Digitized by Google



KALA-AZAR: 1, Free forms from the spleen; 2 and 3, forms in the endothelial cells; 4, in the liver.
ORIENTAL SORE: 5, In endothelial cell; 6, free forms.

PARASITES OF KALA-AZAR AND ORIENTAL SORE.

PLATE XI.

Digitized by Google

Digitized by Google

placed perpendicularly, or at a tangent to the nucleus. It stains more deeply than the latter. In close association with the trophonucleus a small granule, the kinetonucleus, can be made out. The parasites multiply by simple fission, the division of the body being always preceded by the elongation and division of the nucleus and blepharoplast. The plane of division is always longitudinal. Some forms, having attained a larger size, suggest a process of multiple fission; these are almost circular, and present, as a rule, six chromatin masses, three large and three small, the former being placed round the periphery.

The parasites, as they occur in man, are probably almost invariably intracellular. They grow and multiply within the host cell, causing it to enlarge, and then, after disintegration of the nucleus, to disrupt. The parasites so set free either enter other endothelial cells or are taken up by the white blood-corpuscles, in which they are sometimes found in the peripheral circulation. In smear preparations they are often free or in clusters of various numbers, sometimes arranged with great regularity like the merozoites in the segmenting quartan or tertian malaria parasites. Sometimes as many as 50, or 200, or even more parasites are found together embedded in a structureless matrix or stroma, probably the remains of the original host cell.

In cultures (Fig. 56) the parasites enlarge very rapidly. They retain at first their shape, the cytoplasm becoming granular, opaque, and vacuolated. Having attained a diameter of 7 to 9 μ, they assume an elongated pyriform shape and become flagellated. The flagellum arises from the blepharoplast at the rounded end of a parasite, and projects at once clear of the body as in *Herpetomonas*. There is no undulating membrane as in trypanosomes. These flagellated forms measure from 12 to 20 μ in length. They multiply by longitudinal fission, sometimes throwing off exceedingly fine linear forms (Leishman) comparable in their delicacy to spirochætes. They move actively with the flagellum in front, and towards the twelfth day tend to agglomerate in rosette groups, the flagella being directed centrally.

The culture medium used by Rogers was blood to which a small quantity of sterile, slightly acid citrate-of-soda solution was added to prevent coagulation. When the culture medium was kept at blood heat the parasites very rapidly degenerated and disappeared; but when placed in an incubator at 27° C. they lived for three or four days and multiplied. A lower temperature was found to be even more suitable. When temperature was lowered to 20°–22° C. the parasites multiplied more readily, acquired a considerable size,

Digitized by Google

and finally assumed the elongated, motile, flagellated form. The N.N.N. culture medium gives excellent results, and in this, by transplanting at intervals of from twelve to fifteen days, the cultures can be kept alive up to at least four years. The presence of moulds does not affect the cultures, but bacterial contamination is fatal. In experimental kala-azar in dogs Wenyon has noted that characteristic flagellate leptomonas forms may occur sparingly side by side with the typical leishmania, but so far such forms have not been found in the human tissues.

Animal experiments.—The early attempts in India to communicate kala-azar to the lower animals failed, but Nicolle in Tunis, and, subsequently, many others elsewhere, have shown that dogs, cats, jackals, monkeys, rats, mice, and to a less extent guinea-pigs

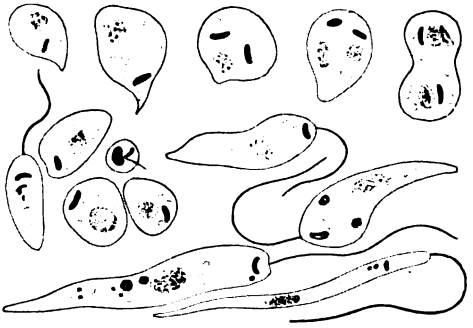


Fig. 56.—Kala-azar parasites in culture. (*After Leishman.*)

and rabbits, are inoculable, provided large doses of the virus are injected into the liver or peritoneal cavity. For a dog, 2 to 4 c.c. of a thick emulsion of infected liver, spleen, or bone-marrow in normal saline usually suffices. Intravenous injection is not so successful. Injection of cultures sometimes succeeds. Archibald succeeded, in Khartum, in infecting a monkey by feeding it on kala-azar material.

Mode of transmission.—This has not been definitely ascertained as regards India, but there is evidence that in the Mediterranean countries the dog* is a principal reservoir of the disease, and may be concerned with the endemicity. It has also been asserted, but not proved, that the dog-fleas, *Ctenocephalus serraticeps* and *C. canis*, are the transmitters. So far as ascertained, as a general rule, wherever kala-azar occurs, there the dogs are infected with

* In the naturally infected dog, symptoms resembling rabies have been noted, by Nicolle, associated with the presence of leishmania in the spinal cord.

Digitized by Google

L. donovani in variable proportion, from 1·8 per cent. to 81 per cent. In India Donovan has failed to find, except in a negligible proportion of instances, naturally infected dogs. Strange to say, although the dog has been found to be susceptible to infection in the Mediterranean area, in India it seems to be partially immune and only contracts the disease after massive intraperitoneal injections of leishmania-infected organs.

The exact way in which the flea transmits the virus, if it be the transmitting agent, is not known—whether the parasite undergoes essential biological changes in the insect, or whether the latter functions merely in a passive or mechanical way.

Patton has put forward a claim for the bug as the transmitter of Indian kala-azar. It may be so, but conclusive proof has not been adduced. Should the conjecture be confirmed, it would afford an explanation of the tendency of the disease to cling to particular localities and houses, and it would supply a valuable guide to prophylaxis.*

Under natural conditions kala-azar, like other diseases caused by similar protozoal organisms, is probably transmitted by a living agent. There are certain facts, however, which tend to suggest that the carrier need not necessarily be a blood-sucking animal. In the first place, the parasite in man is not, as a rule, in great abundance in the peripheral circulation. Secondly, the parasite is often present in ulcerations of the skin and of the intestinal mucosa, suggesting elimination by these organs. Mackie has found leishmania-like bodies in the mucus of dysenteric cases of kala-azar. Thirdly, we know that although some species of *Herpetomonas* are fostered by blood-sucking flies, such as *Tabanus* and *Hæmatopota*, others are found in non-biting forms, such as *Musca*, *Sarcophaga*, *Pollenia*, and *Fucellia*, which could become infected only by settling on ulcerations or on fæcal matter. It is conceivable that such insects might transmit the infection of kala-azar by depositing the parasites on wounds and abraded surfaces. It has been suggested that there is a reservoir for leishmania in some of the lower animals, e.g. the house-lizard. The history of the Assam epidemic is against this view, for it has been definitely shown that the disease was introduced and spread by man, and that it did not pre-exist in the invaded districts, as would have been the case had there been an animal reservoir.

Predisposing causes. — Kala-azar attacks both sexes and all

* The discovery of a flagellated organism or of developing leishmania in the gut of an insect must not be regarded as adequate proof that the insect is a transmitter of the organism concerned, still less that it is the normal transmitter.

Digitized by Google

ages, but, *unlike malaria*, it shows a predilection for the acclimatized—the natives; in them it is said to be as severe and fatal as in the case of new-comers. In the Mediterranean basin it occurs almost though not quite exclusively in children (five months and upwards); in India it occurs at any age.

Incubation period.—This is difficult to fix. In the case of one Englishman, under Manson's care, the time that elapsed from his arrival in perfect health in the endemic region and the onset of the fever which terminated in kala-azar (diagnosed microscopically both before and after death) was under ten days. In a proportion of instances, as in some artificially infected dogs, and as is the case in dermal leishmaniasis, the disease may remain latent for months. In advanced cases in man the parasite may disappear from the tissues before death; what appears to be an explanation of this curious fact has lately been advanced by Archibald, who found certain coccoid bodies by hepatic puncture in these latent cases; he believes that these bodies represent a stage of the parasite. The knowledge of this fact, which has been confirmed recently by Rogers and others in India, renders it probable that many febrile cases of Banti's disease, splenic anæmia, and Egyptian splenomegaly are in reality cases of kala-azar in which the parasite has temporarily disappeared.

Symptoms.—Bentley, speaking from a large experience in Assam, says that the disease commences with high fever, which may be preceded by rigor and, in some cases, by vomiting. This initial fever —intermittent in some instances, more frequently remittent, with a double remission in the twenty-four hours, resembling that of subtertian malaria—may be very severe (Chart 5). It lasts for from two to six weeks, occasionally longer. During its progress the spleen and liver enlarge, increasing and decreasing at first, often in a most remarkable degree, in harmony with the fluctuations of the fever. Then comes a period of apyrexia and general improvement, to be followed once more by fever and splenic and hepatic enlargement, and perhaps tenderness. In this way spells of fever and apyrexia recur for months, absolutely unchecked by quinine, until finally a low form of fever, rarely over 102° F., becomes more or less persistent. Profuse sweats are common during remissions at all stages of the fever; rigor is rare. Pains in the limbs often suggest rheumatism. When the disease is thoroughly established, emaciation and anæmia become noticeable, and, together with the enlargement of the liver and spleen, cause the patient to present a typical appearance. In China a uniform painless enlargement of the cervical lymph-glands has been observed. Œdema of the legs, sometimes

Digitized by Google

circumscribed œdemas, or even ascites* may now be present. In many the skin acquires an extraordinary earthy-grey colour; the hair is apt to become dull, dry, and brittle, and it may fall out; petechiæ, in the axillæ especially, are not unusual; epistaxis and bleeding from the gums are common. This condition of chronic fever, enlargement of spleen and liver, emaciation, and anæmia may continue for months, or even one or two years, until improvement sets in, or more usually—96 per cent. of cases (Rogers), 150 recoveries in 2,000 cases (Price), 24 in 100 cases (Lignos)—until the patient is cut off by an intercurrent disease, especially dysentery (90 per cent.).

According to Rogers, the degree of anæmia, in uncomplicated cases, is usually only a moderate one, the number of red corpuscles being not infrequently over 4,000,000, and, as a rule, over 2,500,000 even in advanced cases.

The most remarkable change seen in the blood is the great and constant reduction in the number of leucocytes. Instead of there being 1 white to about 625 red, as in a normal subject, the proportion is commonly from 1 to 2,000 to 1 to 4,000, and may be lower still. The reduction is most marked amongst the polynuclear variety; the lymphocytes and large mononuclear leucocytes, although greatly reduced in

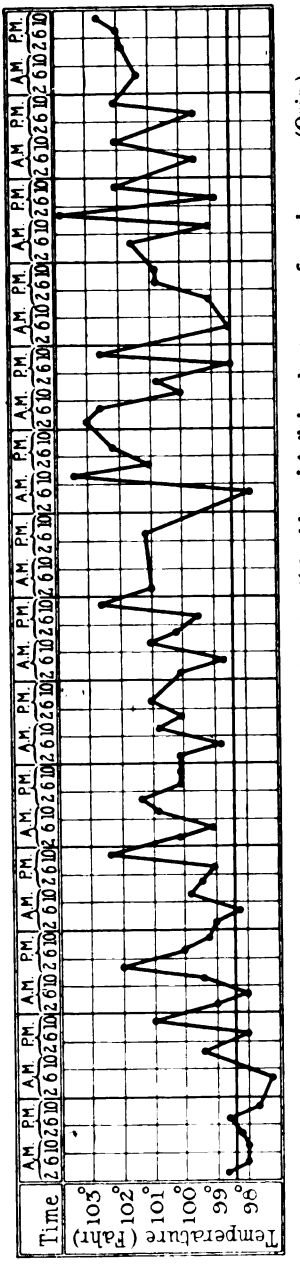


Chart 5.—Four-hourly chart of kala-azar, illustrating the "double crisis" in the twenty-four hours. (*Orig.*)

* Long-standing kala-azar infections may cause a fine fibrosis of the liver and the development of ascites, as originally described by Rogers: perihepatitis and perisplenitis may also be present.

Digitized by Google

number, show a relatively increased percentage, as in some other protozoal diseases. Rogers further states that the alkalinity of the blood is diminished.

In many cases, notwithstanding the chronic fever and progressive wasting, throughout the long illness the tongue is almost uniformly clean and the appetite and digestion are good.

Morbid anatomy.—The *spleen* is greatly enlarged and the thickened capsule may show signs of perisplenitis. The trabeculæ are enlarged, the pulp increased in bulk and full of blood. A section or smear preparation, appropriately stained, will show prodigious profusion of parasitic growth in the crowds of the large mononuclear cells already referred to. The *liver* also is generally much enlarged. It has a brown or mottled section. The parasites are in great abundance, occupying large mononuclear cells, attached or free, in the dilated hepatic and portal capillaries. There may be some cirrhotic changes, but the hepatic cells, though atrophied and perhaps fatty, never contain parasites. The *bone-marrow* is similarly packed with parasite-laden cells. *Intestinal ulceration* is very common, and parasites may be found in the walls of the ulcers as well as in *skin ulcerations* or in the *lymphatic glands*. Occasionally they are found in connection with the blood-vessels in the *kidneys*, but never in the epithelium of the secreting tubules.

Diagnosis.—Irregular chronic fever with enlargement of the spleen and a relative mononuclear leucocytosis in patients from the endemic zone suggests kala-azar. An examination of the blood can at once exclude leucocythæmia and, if taken together with absence of tertian or quartan periodicity and the inefficacy of quinine, malaria. Trypanosomiasis and kala-azar may be difficult to distinguish between, and unless their respective parasites are detected a positive diagnosis is impossible, although geographical considerations and subsidiary skin and lymphatic lesions may assist in forming an opinion.

Splenic puncture must not be lightly undertaken. A preliminary examination of the blood should always be made, not only with a view to ascertain the presence of the Leishman body, but to exclude leucocythæmia and obviate the necessity for splenic puncture, and the attendant risk of fatal hæmorrhage so easily induced in that disease. Death from hæmorrhage may follow this seemingly trivial procedure. When the liver is enlarged, being a less vascular organ and less easily torn, it should be selected for puncture in preference to the spleen. The abdomen had better be fixed firmly with a binder to prevent as far as possible movement of the diaphragm and consequent risk of tearing the punctured organ. A fine hypodermic

Digitized by Google

needle, scrupulously clean and dry,* and connected with the barrel of the syringe by a short length of rubber tubing, should be used, the patient being directed not to start or breathe while the puncture is being made. Failure to draw blood is not to be regarded as failure to obtain material for microscopical examination; on the contrary, it is an advantage, as the object is to procure spleen or liver pulp, not blood. After blowing out the contents of the needle on a slip, a film should be spread and, after it has dried, stained by Leishman's or Giemsa's procedure, and then examined with a $\frac{1}{12}$-in. objective. The parasite is easily recognized by its size, shape, and two chromatin masses.

Wenyon has suggested that culture of the splenic pulp on N.N.N. media gives a higher proportion of positive diagnoses than a simple microscopical examination. In cases of cervical lymphatic enlargement a gland may be excised and examined either in smears or in sections. Certain cases of splenic anæmia, Banti's disease, and Egyptian splenomegaly may simulate kala-azar very closely; in fact, they may be indistinguishable save for the absence of the parasite and the characteristic pyrexia. It is necessary, in making a diagnosis, to exclude visceral syphilis, which, in the enlargement of liver and spleen, may simulate kala-azar. According to Sutherland and Mitra, who examined 38 cases of kala-azar from this point of view, the serums of some 25 per cent. give a pseudo-positive Wassermann reaction, therefore this test is not always conclusive.

Attention must be drawn to a rare disease described as histoplasmosis by Darling in Panama, which clinically resembles kala-azar and is thought to be due to the *Cryptococcus capsulatus*.

Treatment.—Until recently this, as a rule, was unsatisfactory. Although intramuscular injections of atoxyl were attended with a certain amount of success, salvarsan, arsenic, quinine, and even splenectomy, were tried without avail. The intravenous antimony-tartrate treatment, first introduced by Machado and Vianna in Brazil for dermal leishmaniasis, and subsequently applied to kala-azar by Cristina and Caronia, Rogers, Low, and others, has been attended by remarkable results. If instituted before the case has become hopeless, it seldom fails to ensure recovery. Tartar emetic is usually made up in a 2-per-cent. solution, the commencing dose being $\frac{1}{3}$ gr. of the salt, working up to a maximum individual dose of $1\frac{3}{4}$ gr. (5·8 c.c. of the solution). The largest individual dose which can be tolerated is one of 2 gr.

* The presence of a trace of water in the needle will distort or burst the parasite and render it unrecognizable.

Digitized by Google

The injections should be given every third day so as to ensure the cumulative action of the drug. Treatment should be continued for two months after cessation of fever. Knowles, in Shillong, advocates a course of 2 grm. (30·8 gr.), spread over a period of three months, as sufficient for an adult; towards the end of treatment the intervals should be lengthened. For children under 6, 1 c.c. of the solution should be given for the first dose and increased by ½ c.c. up to a maximum of 3 c.c.

Treatment should be continued for two months after the cessation of fever, so as to ensure that no parasites have escaped destruction. Cure, according to Rogers, may be inferred from the absence of fever for some considerable time, a steady gain in weight, and diminution in the size of the spleen.

Improvements have been made recently in the forms of antimony for intravenous injection. Rogers has used sodium antimonyl tartrate, and latterly colloidal antimony sulphide in a strength of 1 : 500, up to 20 c.c., amounting to a total of 2 grm.

The employment of more organic and less toxic compounds of antimony for intravenous injection has given encouraging results. Such a salt is acetyl-*p*-aminophenyl stibiate of sodium (stibacetin). It can be tolerated in larger individual doses, commencing with 0·1 grm. (1·54 gr.), and working up gradually to 0·8 grm. (12·3 gr.). A course aggregating 4 grm. is well tolerated in the few instances in which it has been tried. In the treatment of the infantile form of kala-azar, Caronia, in Italy, has reported favourable results from the intramuscular injection of this salt in doses of 0·15 grm. (2 gr.) up to a total of 3·6 grm. (55·4 gr.), extending over a period of three months.

For young children, in whom neither intravenous nor intramuscular injections are suitable, inunctions of finely divided metallic antimony are advocated.

In every case solutions of antimony salts should be freshly made before use, as stock preparations are liable to decompose.

The particular manner in which antimony acts upon the Leishman-Donovan body is still undecided, for it is known that this parasite may still be cultured from splenic puncture, even when the case is progressing favourably, with consequent shrinkage of the spleen, under treatment.

The toxic symptoms due to antimony are coughing with a feeling of constriction in the chest while the drug is being given, and shortly afterwards vomiting and nausea. The drug is contra-indicated in cases with advanced cardiac or renal disease.

The injection of these toxic compounds should always remain

Digitized by Google

in skilled hands, and doses must be graduated with care. If the solution escapes freely into the tissues, inflammation and even necrosis may result. It is always advisable to flush out the vein, at both the beginning and end of the treatment, with a small amount of normal saline solution.

Finally, the expulsion of intestinal parasites, the treatment of coincident malaria with quinine, change to a healthy climate, good food, warmth, rest, physical comfort, and good hygienic conditions are indicated.

Prophylaxis.—Having regard to the character of the disease, in the endemic districts the cases should be dealt with as infectious; they should be isolated, and their houses and fomites should be disinfected or burnt. Domestic and personal cleanliness is of great importance. Infected dogs and cats should be destroyed; and as far as possible in the endemic districts dogs should be kept free from fleas and not in too close association with man. By segregation of the sick, burning of houses, clothing, and furniture, etc., and provision of new huts, Price, Rogers, and Young have succeeded in exterminating the disease in infected coolie lines.

Oriental sore and kala-azar.—If the parasite of oriental sore be specifically identical with that of kala-azar, it must somehow have been deprived of its virulence; for, although kala-azar is a fatal disease, oriental sore is eminently benign. It is known that one attack of oriental sore confers immunity against further attacks of the same disease. It affects dogs and other animals. May it not be that the virulence of the Leishman body is removed by passage through some animal other than man; or, possibly, by being transmitted by some intermediary other than that which transmits the virulent kala-azar? If this be so, we have at hand a vaccine against kala-azar. The question is worth testing: "Are those who have had oriental sore immune as regards kala-azar, and vice versa?" * In support of this suggestion it has long been recognized in India that in districts where kala-azar is common, oriental sore is rare. Recent work has shown that this is partially true for the Mediterranean area also. In Teheran the dogs are found infected with dermal leishmaniasis, and a general infection combined with cutaneous lesions has been produced in mice by intravenous injections of cultures of *Leishmania tropica* (the parasite of oriental sore), and sores in monkeys by cutaneous inoculation of cultures of *Leishmania donovani*.

* Nicolle has succeeded in producing a certain amount of immunity in dogs and monkeys to oriental sore and to kala-azar by injecting them intraperitoneally with cultures and infected material containing the leishmania of the local and of the general disease.

Digitized by Google

2. Oriental Sore

Synonyms.—Tropical Sore; Bouton d'Orient; Delhi Boil; Cutaneous Leishmaniasis; Salek (Persia), etc.

Definition.—A specific ulcerating granuloma of the skin, endemic within certain limited areas in many warm countries. It is caused by a species of *Leishmania* and is characterized by an initial papule, which, after scaling and crusting over, generally breaks down into a slowly extending and very indolent ulcer. Healing after many months, it leaves a depressed scar. The sore is inoculable and, usually, protective against recurrence.

Geographical and seasonal distribution. — Among the endemic places may be named Morocco, the Sahara (Biskra, Gafsa), the Niger, Egypt, Crete, Cyprus, Sicily, Asia Minor, Syria (Aleppo), Palestine (Jericho), the Sudan, Mesopotamia (Bagdad), Arabia, Persia, the Caucasus, Turkestan, India (Lahore, Multan, Delhi, etc.). Juliano describes the disease as being common in Bahia, Brazil, and cases are reported from Bolivia, Peru, Panama, and French Guiana—where it is called "pian bois," "bosch-yaws," etc. The name oriental sore, suggested by Tilbury Fox, is therefore no longer quite appropriate.

Locally, oriental sore is often called after some town or district in which it is specially prevalent; thus we have Delhi boil, Bagdad boil. "clou de Gafsa," and so forth. It is much more common in cities than in the country. In Bagdad few escape an attack; visitors of a few days only are almost certain, at particular times of the year, to contract it.

In the tropics this form of ulceration is especially prevalent about the commencement of the cool season; in more temperate climates, towards the end of summer or beginning of autumn. Years of prevalence may be succeeded by years of comparative rarity—possibly in harmony with altered sanitary conditions. In Delhi, for example, in 1864 from 40 to 70 per cent. of the resident Europeans were affected with the local sore; on certain sanitary improvements being effected, the frequency of the disease was immediately materially reduced.

History.—In 1885 Cunningham described certain deeply staining parasitic bodies in mononuclear cells derived from these sores; these were again studied in 1901 by Firth, who regarded them as degeneration products. J. T. Wright in 1903 found Cunningham's parasites in great profusion in a sore, and named them *Helcosoma tropicum*. This observation has been abundantly confirmed, so that it is now definitely established that the cause

Digitized by Google

of oriental sore is the Leishman-Donovan body, or at least one morphologically identical. The parasite is termed *Leishmania tropica.*

Etiology.—Section of the papule displays an infiltration of the derma by a mass of small round granulation cells. These lie between the normal elements of the tissue, particularly about blood-vessels, lymphatics, and sweat-glands; towards the centre of the lesion they completely replace the normal structures. The parasites are found in the granulation tissue at the edge of the lesion, and may be demonstrated in scrapings; care must be taken to avoid obtaining too much blood. (Plate XI., Figs. 5, 6.) Occasionally, as recorded by Escomel, flagellating forms of leishmania may be demonstrated.

The cultivation of the parasite, first carried out by Nicolle, is easily effected in the N.N.N. medium. The surface of a non-ulcerating sore is first painted with iodine and then punctured with a fine syringe. The parasites, as in the case of *L. donovani*, grow best in the condensation water. Inoculation of cultures has given rise to lesions in monkeys.

In what way, under natural conditions, the parasite enters the tissues it is as yet impossible to state definitely. Not improbably it is conveyed by flies or other biting insects, and by them either inserted into the skin or applied to some pre-existing wound or sore. The most probable insect carrier would appear to be some species of *Phlebotomus*, though all experimental attempts to transmit the disease through its agency have so far failed. Dogs in Teheran, and perhaps camels, are subject to this or a similar disease; indeed, the *Hippobosca* of these animals has been suggested as a likely vector of this disease in Persia. Monkeys and dogs have proved to be experimentally inoculable, while donkeys, horses, goats, and sheep are refractory. It must not be overlooked that in susceptible animals an important source of infection may lie.

Probably there are two methods of infection—(*a*) *direct*, the Leishman body being directly inoculated without undergoing sexual or other developmental change; (*b*) *indirect*, in which an infected fly, bug, or other insect, either itself or through its progeny, conveys to the new host the parasite which in the meantime has undergone evolutionary changes.* Wenyon has proved that the parasite is unable to enter through the unbroken skin.

* Patton has definitely stated that the bed-bug, *Cimex hemipterus* vel *rotundatus*, is the transmitter of the disease in Cambay, India; these results Wenyon has failed to confirm. It is a mistake to conclude, because a parasite is capable of living for a time and even developing in the alimentary canal of some blood-sucking insect, that that insect is the natural transmitter of the disease. Wenyon has found in the stomachs of mosquitoes, originally fed upon oriental sores, developing forms of leishmania.

Digitized by Google

As a rule, second attacks do not occur. Observing this, the Jews of Bagdad at one time practised on their young children oriental-sore inoculation.

Neither race, nor sex, nor age, nor occupation, nor social condition materially influences susceptibility.

Incubation period and constitutional symptoms.—The incubation period of oriental sore is variously stated in days, weeks, or months. That it may be a brief one, a few days or weeks, seems to be established by the appearance of the sore within a short time of arrival in endemic districts, or after inoculation. That it can be of much longer duration is equally certain. Manson saw an unquestionable oriental sore which did not appear until five months after the patient had been exposed to any possibility of infection. Wenyon inoculated himself with oriental sore in Aleppo; it was not until six and a half months later that a leishmania-containing papule, subsequently developing into a sore, appeared at the site of inoculation. In other cases the incubation period has been as much as fifteen months, or even longer.

There is very little reliable information about the presence or absence of constitutional symptoms. It is customary to describe the disease as non-febrile. This may be true in most cases, but it is not invariably so. It is obvious that in a disease with, at least in some instances, a very prolonged incubation period, slight or even severe fever might be overlooked or misinterpreted. Oriental sore produces an immunity against itself. There must, therefore, be profound constitutional change. In other diseases attended with similar change, fever is almost invariably present at one time or another in their course. In the case just alluded to as occurring in Manson's experience, a severe anomalous fever, of five or six weeks' duration, preceded by eight months the appearance of the local lesions. In Wenyon's case the development of the initial papule was preceded by smart fever supposed at the time to be influenzal. Seeing, as has been pointed out (p. 159), the close connection of oriental sore with kala-azar, this question of the constitutional symptoms in the milder disease is an important one, and should be carefully studied.

Symptoms.—The local lesion in oriental sore commences as a minute, itching papule which tends to expand somewhat as a shotty, congested infiltration of the derma. After a few days or weeks the surface of the papule becomes covered with fine, papery scales. At first these scales are dry and white; later they are moister, thicker, browner, and adherent. In this way a crust is formed, which on falling off, or on being scratched off, uncovers a

Digitized by Google

shallow ulcer (Fig. 57). The sore now slowly extends, discharging a scanty ichorous material; this from time to time may become inspissated, and a crust forms, while the sore continues to spread underneath. The ulcer extends by the erosion of its perpendicular, sharp-cut, and jagged edge, which is surrounded by an areola of congestion. Subsidiary sores may arise around the parent ulcer,

Fig. 57.—Oriental sore. *(After Wenyon, From photo by R. McKay, reproduced in "Journ. Lond. School Trop. Med.")*

into which they ultimately merge. These sores, usually about an inch in diameter, may come, in some instances, to occupy an area several inches across.

After a variable period, ranging from two or three to twelve or even more months, healing sets in. Granulation is slow and frequently interrupted. Often it commences at the centre whilst the ulcer may be still extending at the edge; often it is effected

Digitized by Google

under a crust. Ultimately a depressed white or pinkish cicatrix is formed. Contraction of the scar may cause considerable and unsightly deformity.

Oriental sore may be single or multiple. Two or three sores are not uncommon; in rare instances as many as forty have been counted on the same patient. They are mostly situated on uncovered parts—hands, feet, arms, legs, and, especially in young children, on the face; rarely on the trunk: never on the palms, soles, or hairy scalp. Seidelin, Darling, and Connor have described as occurring in South America oriental sores with a predilection for the margins of the ears.

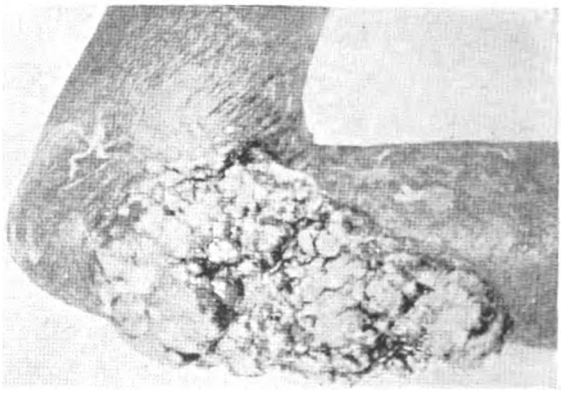


Fig. 58.—Diffuse cutaneous leishmaniasis in an Egyptian. (*Ferguson and Richards.*) (*By permission of the Liverpool School of Tropical Medicine.*)

Sturrock, who practised in Bagdad for four years, informed Manson that in rare instances the disease recurs more than once, but, as a rule, the sores of the second attack do not break down He has also seen a chronic type of the disease, which may recur and persist for several years and be associated with deposit in the testes and in mucous membranes, as well as with a chronic form of dactylitis.

In a very few instances the initial papule does not proceed to ulceration, but persists as a scaling or scabbing, non-ulcerating, flattened plaque—just as sometimes happens in the case of the primary sore of syphilis. Sometimes the ulcer is quite superficial, an erosion rather than an ulcer. Occasionally, from contamination with the virus of some other infectious acute inflammatory skin

Digitized by Google

disease, the primary lesion may become complicated, and perhaps a source of serious danger. Otherwise, oriental sore is troublesome and unsightly rather than painful or dangerous.

A peculiar kind of dermal leishmaniasis has been described by Ferguson and Richards as occurring in Egypt under the name of parasitic granuloma (Figs. 58 and 59). These lesions, which affect the lower extremities, resemble warty outgrowths or papules; they may be solitary or multiple, and may be the result of auto-inoculation. They are best treated by excision.

Fig. 59.—**Diffuse cutaneous leishmaniasis in an Egyptian.** (*Ferguson and Richards.*) (*By permission of the Liverpool School of Tropical Medicine.*)

According to Nattan-Larrier, there is a mononuclear leucocytosis in oriental sore similar to that in kala-azar.

Diagnosis.—On clinical grounds these sores have to be distinguished from the desert or veld sore (p. 699), tertiary syphilis, ulcus tropicum, and blastomycosis. The distribution on the body and the presence of the Leishman-Donovan body render the diagnosis a matter of no very great difficulty.

Treatment.—The best treatment is undoubtedly the intravenous injection of tartar emetic, or possibly sodium antimonyl tartrate, in 2–4 per cent. solution, as already described for kala-azar.

Digitized by Google

This should be done whenever feasible, beginning with ½-gr. doses. Solutions of antimony do not keep well, and they should be freshly made up each time.* Limiting the amount of menstruum prevents severe reactions arising. Local applications of 2 per cent. antimony tartrate in lanolin have been used with success, and are suitable for the treatment of children. The strength may be increased to 15 per cent. According to Greig, antimony may be given by the mouth in the following prescription :

℞	Ant. tart.	gr. v.
	Sod. bicarb.	gr. xxx.
	Syrup	ʒi.
	Aq. chlorof.	ʒi.
	Aq.	ad ʒiii.

Two dr. t.d.s.

Photinos has recently reported good results from local injections of emetine hydrochloride, commencing with 0·15 gr. and increasing gradually up to 1·5 gr., into the base of the sore. A local inflammation is thereby set up, with the disappearance of the parasites from the lesion. The lesions clear up in 15–30 days. Success has been reported with ionization. X-rays and light treatment, CO_2 snow, all have a favourable influence. Methylene-blue ointment, in cases where antimony is unobtainable, may be used in equal parts of the blue, vaseline, and lanolin, applied in a thick layer for fifteen days twice daily. Permanganate of potash may be combined with this treatment in the form of a fine powder, but its application is very painful. Tonics when the patient is anæmic or debilitated, attention to the general health, and change of climate should the disease persist beyond the usual time, are indicated.

3. Leishmaniasis Americana

Synonyms.—Espundia ; Bubas Braziliana, Uta ; Pian Bois ; Forest Yaws ; Nasopharyngeal Leishmaniasis.

Under these names several writers—Carini, Paranhos, Splendore, Escomel, and others—have described a very grave form of leishmaniasis occurring in certain South American countries—Brazil, Bolivia, Peru, Guiana, Martinique, and Paraguay. Christopherson describes a case of the espundia type which he met with in the Sudan, and La Cava has found a similar disease in those parts of Italy in which oriental sore is also endemic. In Paraguay it

* In dispensing solutions of Antimony Salts, special care should be taken to dissolve them in freshly-distilled water. *The solutions should not be boiled ;* this applies especially to the organic compounds.

Digitized by Google

has assumed epidemic characters, and a large proportion of the population in certain districts is said to be affected, so that most drastic public measures have become necessary to prevent its spread.

Symptoms and etiology.—The disease begins as a sore on some mucous surface (Fig. 60). The sore is of the chancrous form of the ordinary oriental-sore type. It heals in time, leaving a

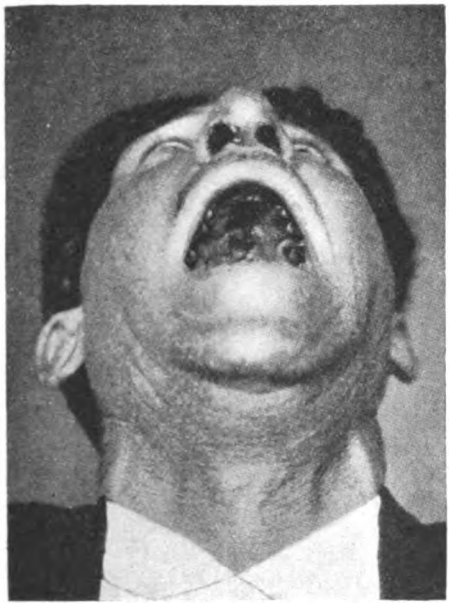


Fig. 60.—Ulceration of hard palate and nares in leishmaniasis Americana. (*After Splendore.*)

characteristic scar. After an interval of months or years, fungating and eroding ulcers (Fig. 61) of a most intractable character break out on the tongue, and in the buccal and nasal cavities, destroying and obstructing them, and ultimately, if untreated by antimony, after years of suffering, leading to the death of the patient by exhaustion. The lymphatic glands are often involved, but the abdominal and thoracic organs are spared.

Leishman bodies are to be found, though not in great profusion, in scrapings and sections of the fungating ulcers, and present no morphological differences from *L. tropica* or *L. donovani*. They have been designated *Leishmania braziliensis*. Giant

Digitized by Google

cells also occur. Dermal ulcers of oriental-sore type may concur with the buccal and nasal lesions. It is believed that the original sore in this grave form of leishmaniasis develops at the site of the bite of a jungle insect of unknown species, possibly a tabanid fly.

Diagnosis is made upon the typical clinical appearances and the discovery of the parasite. Espundia has to be distinguished

Fig. 61.—Ulceration of nares and lips in leishmaniasis Americana. (*After Splendore.*)

from the ulceration of yaws, gangosa, and syphilis, and, in view of this, one must bear in mind that the serum of espundia, according to Ravello, may give a positive Wassermann reaction.

Treatment.—The treatment of this leishmaniasis has now been put upon a sound footing by the work of Vianna, Silva, Escomel, and others. The general treatment is the same as for oriental sore ; 10–20 injections of antimony tartrate generally suffice for a cure. The total amount required for a cure is 1–2 grm. of the salt. The local ulcers on the lips and nose are cleaned up with fomentations and the cleansed surfaces anæsthetized with a mixture

Digitized by Google

of cocaine, menthol, and carbolic acid, then sprinkled with finely powdered antimony tartrate and bound up with a bandage. Subsequently the wounds are dressed with an ointment composed of zinc oxide, bismuth, and lanolin. In the case of the buccal mucosa, scabs must be removed with a solution of bicarbonate of soda, anæsthetized with cocaine (1 per cent.) and sprayed with 1–2 per cent. antimony tartrate solution. Every 4–8 days the tartrate is used in a saturated solution, the application being made by means of a pledget of cotton-wool. Local injections of emetine may also be given a trial.

NOTE.—The student is referred to Laveran's "Leishmanioses" (Masson et Cie.) for a full and accurate discussion of the important and rapidly expanding subject of leishmaniasis.

Digitized by Google

CHAPTER IX

RELAPSING FEVER

Synonyms.—Febris Recurrens; Spirillum Fever; Famine Fever; Tick Fever; Bilious Typhoid of Griesinger.

Definition.—An acute infectious disease, or, possibly, a group of infectious diseases, characterized by fever of sudden onset and, after several days (one to seven), rapid subsidence, and which may relapse at intervals of from one to seven or more days for an indefinite number of times. It is caused by spirochætes which are present in the blood during the fever and are transmitted by certain insects (bug, body-louse) or by certain ticks (*Argas*, *Ornithodoros*).

Geographical distribution.—Relapsing fever is found in Europe, Asia, Africa, America, and probably in Australasia. In Europe it occurs in Britain and, especially, in Ireland; also in Norway, Denmark, Germany, Russia, and Turkey. In Russia there have been many epidemics; it attacked the Grand Army in the retreat from Moscow, the Allied armies in the Crimea, and also the armies of both sides in the Russo-Turkish War. In Africa the disease has long been known in Egypt, the Sudan, and Algeria. Recently, Philip Ross, Milne, and Cook found it in Uganda, Dutton and Todd in the Congo Free State, Wellman in Angola, and Koch in German East Africa. In Asia relapsing fever is known to occur in China, in Sumatra, and in India, where Carter's classical investigations were made. In America it was recognized in the United States in 1844; in 1869 it was epidemic in New York and Philadelphia. It is probably widely distributed throughout South and Central America.

From the symptoms, so far as they are known, and from the fact that in Africa the disease is communicated by tick bite, we are justified in conjecturing that the carapata disease described by Livingstone and Kirk as endemic in the Zambesi basin, the mianeh disease of Persia, and a similar disease described by Alleman in Mexico may be spirochæte-produced diseases, and forms of relapsing fever.

History.—Relapsing fever was known to Hippocrates. He mentions the splenic enlargement, the jaundice, the liability to abortion in pregnant women, and the tendency to menorrhagia.

Digitized by Google

From the time of Hippocrates onwards there is no further notice of relapsing fever in medical literature until 1770; in that year Rutty, in his book on the diseases of Dublin, described it.

In 1873 Obermeier discovered the spirochæte (*Spironema recurrentis* vel *obermeieri*). In 1897 Tictin stated that the parasite and the disease were communicated by the common bed-bug; he infected a monkey with relapsing fever by subcutaneous injection of blood obtained from the stomach of a bug which had previously fed on another monkey inoculated with the disease.

In 1904 Philip Ross and Milne in Uganda, and rather later, but independently, Dutton and Todd on the Congo, discovered that in Africa the spirochæte was communicated by the bite of a tick, *Ornithodoros moubata*. The last two observers found that the parasite could pass into the egg and larva, and so confer infective powers on the mature tick of the succeeding generation. In 1907 Mackie recorded an outbreak of relapsing fever in which lice, *Pediculus humanus* var. *corporis* and *capitis*, apparently served as the transmitting agent—a view favoured by the experiments of Nicolle and others, who further state that the infection can be transmitted hereditarily to the offspring of infected lice.

Etiology.—Experiments and observation have proved that the various forms of relapsing fever are caused by *Spironema recurrentis* or an allied organism, *Spironema duttoni*.

Spironema recurrentis (or *Sp. duttoni*) is a delicate spiral filament (8 to 18 μ by 0·25 μ). Formally, with appropriate staining, a flagellum was described, but this is not now generally accepted as correct (Nuttall). The body of the parasite may have three, four, or six bends or turns; dividing forms appear to have more. By the Romanowsky method the body of the parasite usually stains uniformly, with the exception of the extremities, which are pointed and take only a very faint tint. In fresh blood the spirochætes exhibit very active screw-like movement. Some are longer than others, the long forms resulting from end-to-end attachment of two or more parasites. That this is the explanation of the long forms, which may measure from 16 to 100 μ, is shown by staining. In those measuring from 16 to 18 μ we find a pointed extremity at each end of the filament and a pale zone in the middle, the pale zone corresponding to the approximated lightly staining extremities above referred to. The still longer forms admit of a similar explanation. Although the normal habitat of the spirochætes is the liquor sanguinis, occasionally they are seen within the red blood-corpuscles.

Great variation is shown in the morphology of the spirochætes,

Digitized by Google

and there is a consensus of opinion now that no constant morphological distinctions exist between the organisms occurring in the different clinical forms of the disease.

Demonstration of the parasite.—It is necessary to remember that the parasite occurs in the blood only during the febrile stage of the disease, disappearing often forty-eight hours before the crisis and being absent entirely during the non-febrile intervals. In some forms and cases of the disease it is present in large numbers in every field of the microscope; in other forms and cases it is so scanty that many fields have to be examined before a single specimen can be discovered. In thin films of fresh blood its presence can usually be recognized from the agitation its movements commu-

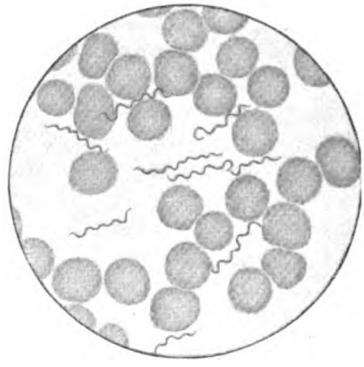


Fig. 62.—Spironema recurrentis in blood-film. × 500.
(*Microphoto: Dr. John Ball.*)

nicate to the adjacent corpuscles. In dried and fixed films the stains in general use for malaria work suffice. (Fig. 62.)

The dark-ground method of illumination is admirably adapted for demonstrating these parasites in a living state; a very strong illuminant, preferably a high-power electric light—not always procurable in the tropics—is required. Occasionally, when very scarce in the bloodstream, as during a relapse, or in the clinical form of the disease met with in North Africa, the organism may best be demonstrated by the "thick drop" method. A film about $\frac{3}{8}$ in. in diameter is made, and after drying is laked with acidulated methyl alcohol (12 drops HCl to 50 methyl alcohol), then stained with aniline gentian violet for twenty seconds.

There is some evidence that the spirochæte is able to break up into granules in the blood, which granules enter red blood-corpuscles and represent a stage in the cycle of the organism. This has

Digitized by Google

been inferred by Balfour from the analogous disease in fowls (*Sp. gallinarum*). These "infective granules" are derived from spirochætes free in the liquor sanguinis, and on entering red cells are believed to complete a cycle of schizogony. According to Balfour, the individual spirochætes about to be delivered of these granules undergo a series of violent contortions, and may be destroyed in so doing. On the other hand, recent observations seem to indicate that the spleen is the natural reservoir of the parasites, and that they return to this organ when they disappear from the peripheral bloodstream.

Systematic position of spirochætes.—The reader is referred to Appendix I. (p. 782) for the classification of these organisms on a biological basis. Suffice it to say that until recently biological opinion was unsettled as to the exact status of the spirochæte—whether it belongs to the bacteria or to the protozoa. Originally it was regarded as a bacterium. The argument for its protozoal nature was founded on its mode of division, which is said to be mainly longitudinal. Recent opinion tends to the former view, and this has been favoured by Dobell, who considers that the argument based upon the hereditary transmission by the tick does not negative its claim to be considered allied to the bacteria.

Cultivation.—The successful cultivation of *Sp. recurrentis*, *Sp. duttoni*, and their subvarieties has been effected by Noguchi, and more recently with simplified technique by Hata in sterile ascitic fluid containing citrated blood and a small amount of fresh kidney incubated at 37° C. The greatest multiplication of the organisms takes place at the junction of the ascitic fluid and blood. The spirochætes reach their maximum development on the seventh to the ninth day, after which they begin to disintegrate.

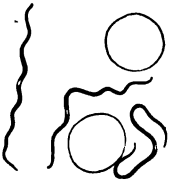


Fig. 63.
Spironema duttoni.

Different strains of relapsing-fever parasites.—Manson first suggested that the different clinical types of relapsing fever met with in different parts of the world were probably due to different varieties of spirochætes; a similar suggestion was made by Sambon, and is borne out by the work of Dutton and Todd upon tick fever. It is now admitted that the spirochætes associated with the different clinical types of fever may be regarded as strains of one species, modified perhaps in virulence by their passage through different intermediary hosts. It has been shown that the strict separation of these spirochætes on the basis of susceptibility of laboratory animals and cross-immunity reactions is untenable.

Digitized by Google

It is undoubtedly the case that in one part of the world the spirochæte of man is transmitted by one species of blood-sucker, and in another part of the world by another species of blood-sucker; that the serum reactions of this spirochæte differ; and that the fevers it causes are in some respects different clinically. It is not justifiable, however, to conclude on these grounds alone that the various strains of pathogenic spirochætes are, in the zoological sense, specifically distinct. It has been ascertained that as regards some of the strains their usual transmitters are interchangeable. It may well be that the continued passage of a given strain through many generations of the same species of insect transmitter may confer on the spirochæte concerned special morphologic and pathogenic qualities, without at the same time transmuting it specifically. Indeed, it would seem that opportunity as supplied by the presence of an efficient insect transmitter, the habits and circumstances of the inhabitants, and the introduction of a pathogenic spirochæte are the principal circumstances that determine the endemicity or epidemic prevalence of relapsing fever; and that the insect transmitter has much to do with the pathogenic qualities of the organism that has been cultivated in its alimentary canal for countless generations.

The parasite occurring in Europe has retained the specific name of *recurrentis*. Novy and Knapp separated the American form under the name of *Sp. novyi*, the Indian form as *Sp. carteri*, the Syrian and Persian as *Sp. berberum*, and the Central African form as *Sp. duttoni*. The main distinguishing points are given in the Table on the next page.

Mode of transmission.—Reference has already been made to the Persian disease called mianeh fever,* and to the carapata disease of the Zambesi valley, as forms of relapsing fever. The former is probably communicated by a tick, *Argas persicus*, and the latter by *Ornithodoros moubata*. In Somaliland it is believed that relapsing fever is transmitted by a second species of ornithodoros—*O. savignyi*. The relapsing fever of Europe is conveyed by lice (*P. humanus*), possibly by the common bed-bug, *Cimex lectularius*, as well; that of India by lice; that of Africa by ticks (*O. moubata*). Proof of transmission by the bug is by no means complete.

There can be no doubt from the experiments of Philip Ross and Milne in Uganda, of Dutton and Todd on the Congo, and of many others, that the African strain, *Sp. duttoni*, is normally conveyed

* A similar anomalous type of relapsing fever was encountered among the troops in Palestine; there was a certain amount of evidence that in this case the transmitting agent was *Argas persicus*. (F. D. Nicholson.)

Digitized by Google

SYNOPTICAL TABLE OF VARIOUS STRAINS OF SPIRONEMA AND CLINICAL SYMPTOMS OF THE RELAPSING FEVERS THEY EVOKE IN MAN

(Compiled from various sources)

	N. Africa and Europe *Spironema recurrentis (obermeieri)*	N. Africa, Palestine, and Persia *Spironema berberum*	Central Africa *Spironema duttoni*	America *Spironema noryi*	India *Spironema carteri*
Animals susceptible ...	Small rodents, only after passage through monkeys.	Gerbils, slightly. Monkey (*Cercopithecus*).	Small rodents and many animals susceptible.	Small rodents very susceptible.	Small rodents infected with difficulty.
Course in animals ...	Mild.	Very mild.	Very severe.	Severe.	Very mild.
Subinoculations in animals	Monkey to monkey, mouse to mouse, positive. (*Fülleborn and Meyer.*)	Gerbil to gerbil, positive.	Monkey to monkey, positive. Same for most animals. (*Breinl, Kinghorn and Garrett.*)	Monkey to monkey, and mouse to mouse, positive.	Monkey to monkey, and mouse to mouse, positive. (*Mackie.*)
Course in man	One, sometimes two relapses. [days Incubation period 5-7 Duration of attack 5-6 Apyrexia . . . 7-10	Fairly severe. First attack 2-8 days; two or three relapses.	Severe—four or five relapses. [days. Incubation period 7-10 Duration of 1st attack 3 Apyrexia 1-8	Mild, rarely more than one relapse. [days. Incubation period 5-7 Duration, 1st attack 5-6 Apyrexia . . . 7-10	Severe, one or two relapses. [days. Incubation period . 7 Duration, 1st attack 5-7 Apyrexia . . . 5-13
Natural transmitters ...	Lice and bed-bug (*Cimex lectularius*).	Ticks (*Argas persicus; Ornithodoros savignyi*).	Ticks (*Ornithodoros moubata*).	Lice (*P. humanus*). .	Lice and bug (*Cimex hemipterus (rotundatus*).
Serum reactions	Immune serum not agglutinating *Sp. noryi* or *Sp. duttoni*.	Immune serum not agglutinating *Sp. recurrentis*.	Immune serum not agglutinating *Sp. noryi* or *Sp. recurrentis*.	Immune serum not agglutinating *Sp. recurrentis duttoni* or *Sp. carteri*.	Immune serum not agglutinating *Sp. noryi*.

NOTE.—This classification can be regarded as provisional only; the recent experiments on cross-immunization render it probable that pathologically, at any rate, the organisms show varying degrees of virulence.

Digitized by Google

by the tick *Ornithodoros moubata*, and that it can be transmitted not only by the animal that has bitten the infected individual, but by its progeny. The spirochæte has been demonstrated in the egg of the tick by Dutton, Todd, and Koch; and Leishman describes certain groups of "coccoid bodies," which may have been derived from spirochætes, in the same situation. It may be that in this way the hereditary transmission of the spirochæte in ticks and lice is effected. Leishman reports that the spirochætes are commonly found in ticks' eggs laid in the tropics, but not in those laid in this country. Balfour believes that the eggs contain his infective granule. Symptoms of a successful infection by the tick appear in from five to seven days.

According to Leishman, the spirochætes remain motile for several days after ingestion by the tick (*O. moubata*), the duration of this depending upon the atmospheric temperature; they then lose their motility and break up into chromatic granules which clump together in the Malpighian tubules of the tick. Should the temperature be raised, a crop of young spirochætes develop from the granules and then disappear suddenly. It would appear that recurring multiplication of the spirochætes takes place in the tissues of the tick in much the same way as in man. The Malpighian tubes act in this case as a culture-tube, the organisms being subsequently passed out in the fæces of the insect. The entrance of the spirochæte into the human skin is aided by the irritation caused by the bite, which provokes scratching and consequent inoculation of the deposited spirochæte; this is facilitated by the fluid exuded from the tick's coxal glands which dilutes the fæces.

All the evidence collected in the War (i.e. in Egypt, Serbia, Russia, and Germany) tends to confirm Nicolle's view that the louse (*Pediculus humanus*) is the chief transmitter of the European and North African form, and that a similar cycle takes place within the body of that insect.

After imbibing blood, the spirochætes disappear rapidly from the alimentary canal of the louse for 2-6 days, but reappear in the cœlomic fluid on the ninth day. It is said that 42 per cent. of lice fed on spirochæte-containing blood become infective, although at this time spirochætes cannot be demonstrated within their body cavities. Apparently, in the case of the louse, infection of the human host takes place through the louse being crushed upon the excoriated skin. It is generally stated that neither in the louse nor in the tick is the infection conveyed by the bite of the insect, though in the case of the former the evidence is by no means so clear. Da Rocha Lima conveyed relapsing fever to a volunteer

Digitized by Google

by lice by means of an experiment in which the possibility of infection through the fæces was excluded.

There is no conclusive evidence, so far, that in the case of the louse hereditary transmission takes place, though da Rocha Lima's recent observations are suggestive. He has demonstrated spirochætes in the walls and lumen of the oviduct and evidently entering the ova. In the case of *O. moubata* the hereditarily infected nymph can communicate the disease. The tick itself has been shown to be infective up to a year and a half after the initial feed on spirochæte-containing blood.

Animal experiments.—It used to be generally stated that *Sp. recurrentis* could be transferred only to man and monkey. Novy and Knapp infected white mice and white rats. The former, they found, were especially susceptible, the organism appearing in the blood within twenty-four hours of inoculation and persisting to the third day. About this time they disappear for several days from the blood until the commencement of the first relapse, which may be followed by a second, third, or even a fourth, the number varying in individual mice ; with each relapse the parasites reappear in the blood. The interval between the relapses is generally about seven days ; occasionally it is only two, though it may be as many as ten. The actual number of organisms in the blood in the first is greater than in subsequent relapses, indicating the development of a partial immunity. Recovery in mice is the rule.

The same observers found rats to be susceptible, but in them the progress of the disease was different. The period of incubation was longer (forty hours), and there were no relapses. As a result of the consecutive passage of the spirochætes through a long series of rats its virulence was augmented, so that the incubation period became reduced to fifteen or eighteen hours, and the persistence of the parasite in the blood prolonged to sixty hours instead of, as originally, forty-eight hours ; at the same time the spirochætes became far more abundant.

The parasite, which is present not only in the circulating blood but in all the organs, seems to produce no serious pathological change in the rat beyond great temporary enlargement of the spleen. Recovery is practically invariable. Young are more susceptible than old rats. The immunity thus acquired persists for many months.

Rabbits and guinea-pigs are refractory.

Immunity.—Sabritschewsky in 1896 showed that when equal parts of spirochæte-infected blood, or serum, and normal serum are mixed, the spirochætes survive longer than when the infected

Digitized by Google

blood is mixed with that of an individual who has recovered from relapsing fever. He accordingly concluded that the cause of the crisis in relapsing fever and of subsequent immunity was the development of a germicidal substance in the blood. He was the first to apply serum-therapy in the treatment of relapsing fever. He obtained an anti-spirochæte serum by repeated inoculation of the horse with human spirochæte-containing blood. The value of this serum was successfully established by Löwenthal; of 87 patients treated, 43 (49 per cent.) recovered without a relapse.

Novy and Knapp have confirmed the presence of a powerful germicidal substance in relapsing-fever blood by comparing the viability of the spirochætes in blood taken (1) at the onset of the disease, (2) during crisis, (3) twelve to twenty-four hours after disappearance of parasites, and (4) from animals hyperimmunized by repeated infection. In the case of the first, the spirochætes live and are motile for forty days, and the blood will continue infective up to thirty-seven days; in the case of the second, no living spirochætes are to be found after twenty-four to forty-eight hours; in the third, the parasites die in from thirty to sixty minutes; in the last, they are killed instantaneously.

They further showed, by examining the blood during the decline of the fever in an infected animal treated with immune blood, that the presence of agglutinating and germicidal bodies could be demonstrated *in vivo* from hour to hour. The parasites are seen to form agglutination rosettes and filaments of 70 μ to 100 μ in length.

Treated *in vitro* with hyperimmune serum, the spirochætes rapidly become unrecognizable aggregations of granules.

European, North African, American, and Indian types. *Symptoms.*—The incubation period of all clinical types usually lasts from two to ten days. In some instances the attack develops promptly on exposure; it is never delayed beyond the fourteenth day. In the artificially inoculated, symptoms show themselves in from two to six days.

The onset is generally abrupt, being marked by chilliness or rigor, giddiness, epistaxis, vomiting, photophobia, and intense headache. In the young there may be convulsions. Temperature rises rapidly to 104° or 105° F., sometimes even to 108°. The pulse is rapid, 110 to 130. Should fever run high there may be delirium. The skin is dry, although, especially during the first day, occasional sweats may break out. A slight icteric tinting of the conjunctiva is usual; not infrequently jaundice is

Digitized by Google

marked at the crisis. The spleen is invariably enlarged and tender. The tongue is coated and moist, except in bad cases, in which it may become dry and brown. The bowels, as a rule, are confined; abdominal pain may be considerable. Occasionally herpes labialis is noted, and in certain epidemics a rash of rose-coloured spots on the trunk and limbs has been observed; some authors describe petechiæ. This rash has a peculiar distribution, being generally confined to the region round the neck, spreading in a semicircular fashion from the tips of the mastoid processes; thence it ranges in a symmetrical manner round the shoulders, down the sides of the chest and abdomen to the inner aspect of the thighs, and to the extensor and flexor aspects of the forearms. The individual petechiæ may be as large as a threepenny bit and need to be carefully differentiated from the exanthems of typhus and hæmorrhagic smallpox.

A slight bronchitis is not uncommon. The urine, not appreciably diminished in amount, is very high-coloured. It generally contains a small amount of albumen, and, it may be, red cells and leucocytes. According to Dudgeon, spirochætes may be demonstrated in it in 30·3 per cent. of cases.

This, the primary remittent fever, lasts from five to seven days. At first the morning is usually lower than the evening temperature, but on or about the third day the evening temperature rarely rises above that of the morning. On the fourth, fifth, or sixth day there is again a rise of temperature, sometimes with delirium, ending in crisis of profuse sweating and diarrhœa. The temperature now falls rapidly to normal or subnormal, sometimes dropping in the course of a few hours as much as 12° F.; in the latter event, especially in elderly or delicate patients, there may be dangerous collapse.

The initial pyrexia, called *first paroxysm*, is followed by a *first period of apyrexia* during which the patient recovers so rapidly that after four or five days it may be difficult to keep him in hospital. But from seven to nine days after the crisis, that is about the fourteenth from the commencement of the attack, rigor again occurs, followed by a second attack of fever—*first relapse*. This may be more severe than the initial paroxysm; usually it is milder and seldom lasts so long. During its continuance the secretion of urine is considerably increased; sweating also is profuse and prostration marked. A polymorphonuclear leucocytosis of 15,000 and over is found during the pyrexial periods.

With the defervescence of the first relapse the patient enters on the *second period of apyrexia*, which is usually coincident with

Digitized by Google

convalescence. (Chart 6.) But in some patients a *second relapse* may occur, usually about the twenty-first day counting from the commencement of symptoms. This second relapse rarely lasts longer than three days, and is generally milder than the previous paroxysms. In rare instances three, four, five, or even more relapses have been observed. Anomalous types of fever are common. One has seen temperature charts with an intermittent fever throughout, more resembling that of phthisis than anything else. Cases with four relapses in a period of twenty-six days are met with. Occasionally the apyrexial period may be of considerable length—seventeen days; in one case observed, forty-two days.

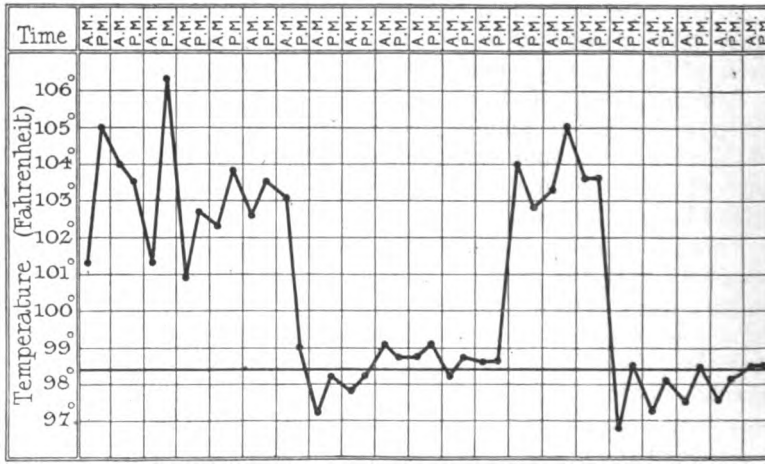


Chart 6.—Relapsing fever, European type. (*Orig.*)

Convalescence may be protracted, and complicated with such sequelæ as nephritis, ophthalmia, otorrhœa, polyarthritis, pneumonia, neuritis, parotitis, adenitis. In pregnant women abortion is the rule.

Severe or fatal cases become stuporose with development of tympanites, hiccough, and severe diarrhœa. These severe forms are more generally seen in war time, when, in the presence of starvation and exhaustion, the disease assumes a more serious aspect.

Palestinian and Persian type (mianeh disease).—This type is said to be due to the strain of spirochætes named *Sp. berberum*, and to be conveyed, in certain districts at any rate, by the tick *Argas persicus*. It is common in Persia, Palestine, and Syria, and resembles the anomalous types of relapsing fever met with in

Digitized by Google

Algeria, Somaliland, and the Sudan, where it is possibly carried by an ornithodoros (*O. savignyi**).

Symptoms.—These may be said to be intermediate between those of the European type and those of the Central African type; in that, as compared with the European, the relapses are more numerous and of shorter duration, while the organisms are very scanty in the peripheral blood, requiring a thick-drop method for their demonstration. (Chart 7.) These cases were frequently encountered among the troops in Palestine and in East Persia (Harold). The attack is generally a very mild one; the initial pyrexia shows marked morning intermissions and lasts four to five days, when the

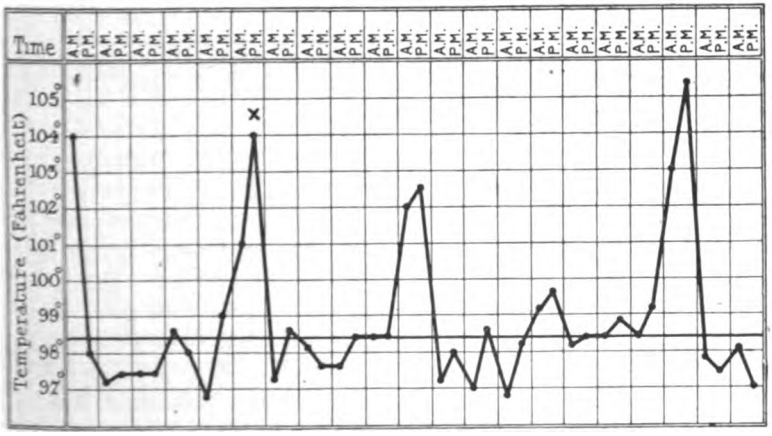


Chart 7.—Relapsing fever, Persian type. (*Bellingham-Smith.*)
x Spirochætes demonstrated in blood-film.

temperature comes down either by lysis or by crisis. Three, four, five, or even more relapses are often noted, individual relapses lasting sometimes only twenty-four hours, or, at a maximum, three days. The spleen is rarely enlarged, and icterus does not occur as a rule.

During the paroxysms there is a leucocytosis of 10,000 or over; recent investigations tend to show that it is the mononuclear rather than the polymorph cells which may be affected.

Central African type (carapata disease; tick fever).—The African tick-conveyed spirillum fever, caused by *Sp. duttoni*, although, as regards the type of fever, resembling the classical

* Under experimental conditions Brumpt has succeeded in transmitting relapsing fever through this species, but the infection does not appear to be hereditary in this species, as it is in *O. moubata*.

Digitized by Google

European and Indian forms, differs from these in some important particulars. The initial fever is not usually so prolonged, generally terminating in crisis within three days. Diarrhœa and dysenteric symptoms are not uncommon. The apyretic intervals are of very irregular duration, being, according to Philip Ross, sometimes as short as one day, sometimes as long as three weeks; and instead of only one or two relapses, as in ordinary relapsing fever, there may be as many as eleven; five or six relapses are the rule. (Chart 8.) The fever, though shorter, is as severe in the relapses as in the initial paroxysm, but the intervals tend to become longer. In some instances the reverse is the case, and this perhaps in both particulars. Sometimes the fever may assume a low chronic

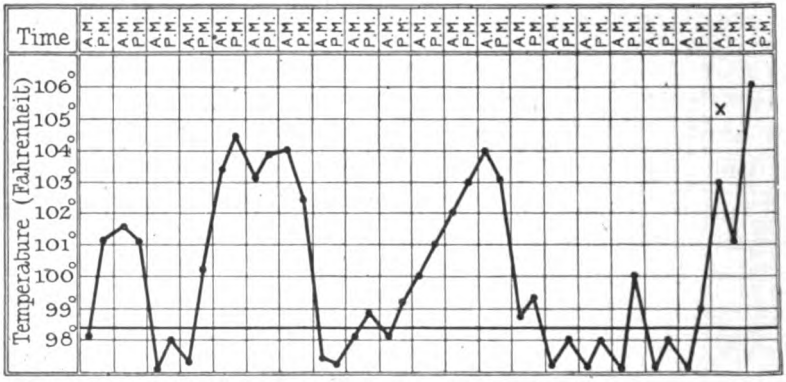


Chart 8.—Relapsing fever, Central African type. (*After Newham.*)
x Spirochætes present.

form, it may be with severe headache and vomiting. Iritis is not an uncommon complication or sequela. The liver and spleen are generally enlarged, and bronchitis and pneumonia are frequent complications. As already stated, the parasites are usually very scanty in peripheral blood, and may be hard to find. There is a polymorphonuclear leucocytosis, as in the European type, and a slight aplastic anæmia.

Fulminating cases, in which the onset is very sudden, were observed nine times in a study of 1,500 cases during the East African campaign by J. K. Manson and Thornton. In these the spirochætes occur in enormous numbers; coma and death may ensue within twenty-four hours. Sometimes there is most intense icterus. These observers consider that death is brought about by the impaction of masses of spirochætes in the cerebral capillaries.

Digitized by Google

In natives of the endemic districts the disease, as generally observed, is not nearly so severe as in Europeans and strangers, being usually limited to a paroxysm or two of one or two days' duration. The mildness of these attacks is probably explained by a partial immunity conferred by previous attacks.

In native races J. K. Manson and Thornton have shown that implication of the central nervous system is a not uncommon complication of tick fever. They have described aphasia, facial paralysis, hemiplegia, and implication of the cranial nerves—such as the third, fourth, and sixth (resulting in ptosis and strabismus), the fifth (trigeminal neuralgia), the seventh (facial paralysis), and the eighth (deafness)—as coming on suddenly during the course of the disease.

Mortality.—The death-rate is usually below 6 per cent. In the feeble and old, death may take place at the height of the first paroxysm.

Diagnosis.—This fever is most usually confounded with subtertian malaria, from which it is often indistinguishable on clinical grounds; it may resemble infectious jaundice, enteric, typhus, influenza, dengue, pneumonia, malignant smallpox, and even plague. In South America it may be confused with yellow fever. The detection of the spirochætes with the microscope, or by animal inoculation, is the most reliable method of diagnosis. At an early stage, the relapsing character of the fever not having declared itself, this feature is not available as an aid to diagnosis, but at a later period the history of a fever which had relapsed about fourteen days from the commencement of the disease should be regarded as highly suggestive of relapsing fever.

Wassermann reaction.—A strong positive complement-deviation (p. 913) is given, both during the pyrexial stage and in the apyretic periods between the early relapses, in about 20 per cent. of cases (Fairley). This apparently applies to all clinical types of the disease.

Morbid anatomy.—The spleen is usually large and soft, and often shows multiple infarcts. It may rupture spontaneously during life. Liver, kidneys, and heart show cloudy swelling of their cellular elements. The skin in fatal cases is usually jaundiced, and there may be submucous petechiæ. The bone-marrow is hyperæmic and shows great activity of the leucoblastic elements (Fairley and Dew). There is generally a marked polymorphonuclear leucocytosis, and the spirochætes are present in large numbers—often phagocytosed—in the spleen and bone-marrow.

Digitized by Google

Treatment.—Careful nursing and dieting are necessary, especially in the African type, and must be maintained after the crisis, when the patient is ravenously hungry. Fortunately we possess a specific in *salvarsan and its allied preparations*. They should be given by the intravenous route in doses of 0·3 grm. to 0·9 grm., according to the age of the patient and the severity of the case; after a short aggravation of the symptoms a crisis takes place with the disappearance of the spirochætes from the blood, and, in the vast majority of cases, recovery. Should relapse occur—a rare event—a second injection may be given. Of the salvarsan compounds, undoubtedly novarsenobillon is the best; neosalvarsan, luargol, kharsivan, galyl (0·35 grm.), and salvarsan are useful in a descending order of merit. Evidence shows that the compound is most efficacious when given in the precritical stage—that is, when the temperature is on the rise, directly the diagnosis has been made. Relapses are apt to occur if it is given while the temperature is *on the fall*, or during the apyretic period; this is especially true of the Central African type. If it is not given in the first attack, one should wait till the first relapse, and then give it on the rise of temperature. It must be remembered that salvarsan ought not to be given immediately before the crisis: a very grave reaction, due to the great destruction of the spirochætes and the liberation of their toxins, with corresponding aggravation of the symptoms and, it may be, fatal collapse, is apt to ensue; on the other hand, the great majority of otherwise healthy patients recover without any treatment at all. Albuminuria in this disease should not constitute a contraindication to salvarsan treatment.

Methods of administering salvarsan, novarsenobillon ("914"), and salvarsan compounds (dioxy-diamino-arsenobenzene-monomethylene-sulphoxylate of soda).—Novarsenobillon is sold as a yellow powder hermetically sealed in glass phials. It may be given intravenously or intramuscularly.

Of these the intravenous is the one to be recommended; intramuscular injections are very painful and may be followed by sloughing.

For *intramuscular* injection a solution of the drug is made in ½ c.c. of sterile distilled water and made up to 2 c.c. with creo-camph, melting at 15° C. Solution is effected by dissolving the novarsenobillon in the prescribed quantity of water in the barrel of the syringe; the creo-camph is then added and the mixture well shaken. Injection is generally made into the buttocks: the dose is 8–10 gr. (0·5–0·64 grm.) in the male, 7 gr. (0·4 grm.) in the female; in children ½ gr. (0·03–0·04 grm.) for each year of age is taken as the standard. The injection should be made above the great trochanter, three fingers' breadth below the ilium.

For *intravenous* injection the glass phial containing 0·9 grm. is taken, the contents carefully added to 50 c.c. of *freshly* distilled water (in the original salvarsan compound it was necessary to add 18–23 drops of 15-per-cent. soda solution till a precipitate formed). In well-developed subjects

Digitized by Google

it is not necessary to expose the vein; the median basilic or cephalic can easily be made to stand out prominently by compressing with a rubber bandage or by the hand. The intravenous needle, preferably fitted with a two-way tap, can be introduced direct. Attached to the needle is a funnel with a glass-joined rubber tube; care should be taken that both are filled with saline beforehand and all air excluded by raising the lower end before introduction. The vein should be flushed out with 10–20 c.c. of normal saline preliminary to running in the drug, to ascertain that everything is in working order. Finally, a similar amount should be given after the novarsenobillon (salvarsan or neosalvarsan, etc.), to prevent any leakage of the solution into the wound, which might cause inflammation or even abscess-formation. Most authorities are averse to using too large a quantity of saline for this purpose, as being apt to cause too great a subsequent reaction.

Atoxyl, antimony tartrate, mercury salicylate, quinine, and methylene-blue are of no avail in relapsing fever.

A mixture called "satoxyl" (atoxyl 10 grm., perchloride of mercury 0·3 grm., iodide of potassium 2·5 grm., distilled water 100 c.c., in doses of 3·4 c.c. given *intravenously*) has acquired a local reputation in the treatment of African tick fever, but recent reports are not confirmatory.

Serumtherapy.—Novy and Knapp have proved that passive immunity can be imparted by the injection of hyperimmunized blood, and that both active and passive immunity persist for several months. Preventive inoculations have been successfully practised on animals. It is possible that we have in this a basis for the prevention of relapsing fever in man.

Prophylaxis.—In the lice-conveyed forms of relapsing fever, prophylactic measures are necessarily aimed at the destruction of lice and their eggs by all the measures known to sanitary science—often a matter of very considerable difficulty when dealing with large bodies of native porters or labourers, especially during the rainy season. This is best performed by means of superheated steam in a portable Thresh's disinfector, or in specially constructed cars in a disinfecting train, the superheated steam being supplied by the locomotive (Stammers).

In the case of the African form, prophylactic measures are much more difficult, and necessitate an intimate knowledge of the habits of *Ornithodoros*, which does not live on the body of its victim, but emerges at night time from the native houses to feed on blood. The following rules are necessary:—

1. Avoidance of native houses, most of all at night-time—especially those situated on much-frequented routes of travel. Native bedsteads should also be avoided. Camps should be placed as far distant as possible from native villages.

Digitized by Google

2. Avoidance of much-frequented ground for camping sites; it must be remembered that *Ornithodoros* can exist without food for years. Sleeping on the ground should not be practised unless absolutely necessary, and only when well protected by a mosquito-net. The use of a nightlight is recommended to scare away the ticks. Blankets should be carefully inspected before retiring to rest.

Native huts should be so constructed that a space of 8–10 in. intervenes between the walls and the ground. Mud and rubble buildings are inadvisable; floors should be raised, and made of cement. A deep trench dug round a building and filled with wood-ash has been found effective in excluding ticks.

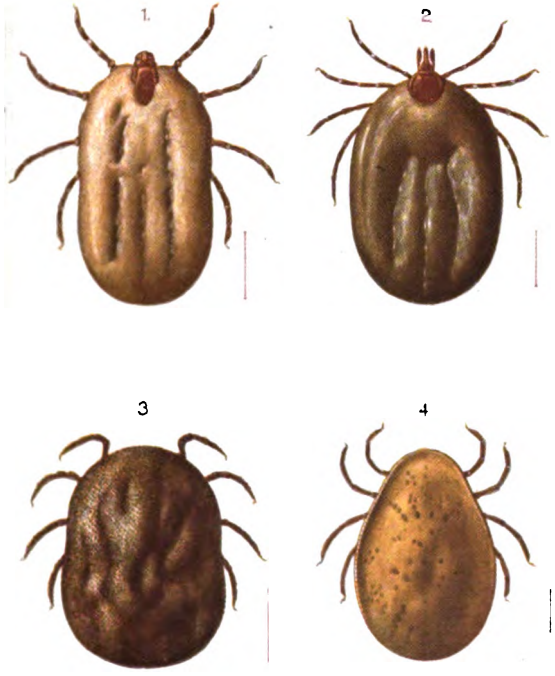
Relapsing fever may be acquired by direct infection, and care is necessary in injecting patients with salvarsan to guard against contact with spirochæte-containing blood. Cases have occurred in which hospital attendants have become infected through an abrasion of the hands, and even from the entry of blood into the conjunctival sac.

Ticks

Recent developments in human and veterinary pathology have shown that ticks play an important part in the transmission of disease. They are widely distributed, almost every animal either having species special to itself or being liable to attack by species of a wider zoological range. They belong to the order of the *Acarina*, of which they are by far the largest forms; their zoological affinities are dealt with in Appendix II., p. 857. They are always visible to the naked eye, and the females are almost invariably larger than the males. In some species the ovigerous females, when gorged with blood, may reach a length of nearly half an inch. As a rule they are temporary parasites, but some live in a quasi-permanent manner on the body of their host; and occasionally a few, as the sheep tick, *Ixodes reduvius* (Plate XII., 2), may even burrow beneath the skin. They differ from insects in possessing four pairs of legs, and in having the three regions of the body—head, thorax, and abdomen—fused into one inarticulated mass. This latter feature also distinguishes them from the spiders, in which the abdomen is clearly distinct from the cephalothorax.

After impregnation the female tick attaches herself to her host. Becoming enormously distended with its blood, she drops off and secretes herself in some convenient hiding-place where she deposits her eggs, which are small, yellowish, roe-like grains, amounting in some cases to thousands. Oviposition begins from two to ten days after the host has been quitted, and goes on for several days. In due course (two or three weeks under favourable conditions) the eggs are hatched. The larvæ look like minute moving grains of sand. They are characterized by having only three pairs of legs, no stigmata, and no sexual orifice. A suitable opportunity presenting, the larva attaches itself to a vertebrate host. After a period of growth it goes through a first moult (ecdysis), and emerges from its larval skin as a *nympha*, provided with

Digitized by Google



1, Margaropus (Boophilus) annulatus (partially distended); 2, Ixodes reduvius (partially distended); 3, Ornithodoros moubata; 4, Argas persicus.

TICKS. ♀.

PLATE XII.

Digitized by Google

Digitized by Google

eight legs instead of six, and with a pair of large stigmata placed, one on each side of the body, behind the fourth pair of legs. After a second period of growth and a second moult it becomes sexually mature. In some species, as in the case of *Margaropus bovis*, the metamorphosis from larva to nymph, and from nymph to imago, takes place upon the same host, the parasite remaining attached during the process. In other species, as in the case of *Hæmaphysalis leachi*, the tick, before each moult, drops off as soon as it ceases feeding, and in consequence has to find a host three times during its life, instead of once. Having reached maturity, the sexes unite. After fertilization the male dies, but the female proceeds to engorge herself with blood for the development of her ova.

On account of the difficulty of finding an appropriate host, ticks at all stages are endowed with a phenomenal capacity for fasting. Megnin found *Argas persicus* alive after a fast of four years' duration.

Ticks are referable to two families, the *Ixodidæ* and *Argasidæ*, differing both in structure and in life-habits. Their characteristics and generic classification are indicated sufficiently for practical purposes in the synopsis in the Appendix.

The species of interest to the human pathologist are *Ornithodoros moubata*, *O. savignyi*, *Argas persicus*, and *Dermacentor venustus*—the first two being the transmitters of the spirochæte of African relapsing fever; the third, of the spirochæte of the mianeh disease; the fourth, of the germ of Rocky Mountain fever. Other species will in the future probably be found to be concerned in the transmission of disease germs to man. Important animal diseases due to *Spirochætæ* and *Babesiæ* are also known to have tick transmitters. *Spironema gallinarum* of fowls in Brazil is transmitted by *Argas miniatus*. *Babesia bigemina* (*bovis*) is conveyed in various countries by different species of *Margaropus*, such as *M. annulatus* (Plate XII., 1), *M. australis*, *M. decoloratus*; *Theileria parva* by *Rhipicephalus appendiculatus* and *R. simus*; *Babesia ovis* by *R. bursa*; *Nuttallia equi* by *R. evertsi*, and *Babesia canis* by *Hæmaphysalis leachi* and *Dermacentor reticulatus*.

Ornithodoros moubata (Murray) (*O. savignyi* var. *cæca*, Neumann) is extensively distributed throughout tropical Africa (Plate XII., 3). Its body is rotund and oval in outline. Its colour, when alive, is greenish brown. The integument is hard, leathery, covered with close-set shining granules or tubercles, and marked both above and below with symmetrically arranged grooves. The females may attain about 8 mm. in length by 6 to 7 mm. in breadth, and moult frequently. This species is widely distributed in Africa, from Uganda and Somaliland in the east, and Congo and Angola in the west, to Namaqualand and the Transvaal in the south.

In habit *Ornithodoros moubata* resembles the common bed-bug. It lives in the huts of the natives, hiding during the day in cracks in the walls and floors, or in the thatched roofs, and moving about actively during the night in search of nourishment. It attacks both man and beast. It feeds slowly, and would be unable to get much blood from any but a sleeping person. Dutton and Todd observed that a big female might remain, firmly fixed, feeding on a monkey for two or three hours before it finally dropped off, distended to the size of a cherry. *O. moubata* deposits its eggs in batches of fifty, seventy, or a hundred. Dissection has shown that only a few eggs mature at a time. The fertility of the female is favoured by liberal feeding. The females lay batches of eggs after each feed, but do not continue to moult. The eggs hatch in about twenty days. In the case of this tick, Dutton and Todd have observed that the larval stage is practically omitted. About

Digitized by Google

seven days after oviposition the hexapod larva can be seen to be forming within the translucent egg-shell. About the thirteenth day the egg-shell splits, and about the same time the larval skin splits also, and the eight-legged nymph throws off simultaneously both the egg-shell and its larval skin. There are several nymphal stages; the exact number has not been clearly ascertained. The largest nymphs may equal adults in size, and show a punctiform mark where the sexual orifice is situated in the adult.

An interesting feature, and one perhaps having a bearing on the etiology of tick-transmitted diseases, pointing as it does to a channel by which the eggs may receive a germ ingested by the parent, concerns certain cells in the stomach wall. The tick, while feeding, from time to time expels per anum a whitish material. This excretion is derived partly from the Malpighian tubes, and partly from the cells alluded to. In the stomach wall, nourished by the imbibed blood, these cells elongate towards the cavity of the ventricle; the other end, smaller and becoming clavate, splits and emits the elaborated nutriment into the general body cavity, where it mixes with the blood of the tick. The cell then, becoming globular, drops into the lumen of the stomach, constituting part of the white excretion expelled per anum. One can readily understand how, by the former route, a parasite could reach the tissues of the tick, including the ovaries. Balfour has infected chickens with *S. gallinarum* by feeding them on eggs of infected *Argas miniatus* (*persicus*).

O. moubata is especially common along the routes of travel. The rest-houses are always the most infested. The ticks are frequently carried long distances in mats or bedding, or in porters' loads which have been piled for safety in the rest-huts at night.

The natives of some places, and also the Boers, protect themselves by plastering their huts, both floors and walls, with mud and cow-dung. The huts are also frequently smoked in order to drive the ticks from the thatch. A most valuable remedy for immediate use is the powder of the pyrethrum flower, which should be dusted between the sheets of the bed. Some protection may be obtained by keeping a lamp alight by the bedside throughout the night.

In certain parts of Africa the distribution of *O. moubata* is overlapped by that of a closely allied species, **O. savignyi**, which is more diurnal in its habits and seems to have a predilection for market-places, cattle-stands, etc. *O. savignyi* differs from *O. moubata* in being provided with eyes, in having larger processes on the legs and a more minutely pitted dorsal surface. *O. savignyi* has been recorded from Egypt, Nubia, Abyssinia, Somaliland, British East Africa, etc., as well as from Southern Asia. It also may be concerned in the transmission of African relapsing fever or other disease. Its bite is dreaded by the natives.

Argas persicus (Fischer), *A. miniatus* (Koch) (Plate XII., 4), has a flat, thin, oval body of a yellowish, greenish, or reddish colour, spotted on the back with a great many white granulations; the legs are pale yellow. Its distribution is cosmopolitan; it is found more commonly in the north and east of Persia, also in Syria, Turkestan, Russia, China, Algeria, and Cape Colony, in North and South America and the West Indies, West Australia and Queensland. It attacks both poultry and human beings. Its habits are similar to those of *Ornithodoros moubata*; it infests old houses, living in the cracks of walls and floors. Kotzebue says that in Persia, as in the case of Mianeh, on the Teheran-Tabriz road, it may so infest villages as to drive out the inhabitants.

Digitized by Google

Bronchial Spirochætosis

In a chapter on tropical spirochætoses one must include a brief description of a bronchitis associated with blood-stained sputum, attributed by Castellani to the presence of a spirochæte, *Spironema bronchiale*, in the expectoration, and which has attracted attention during recent years.

A number of papers by Castellani, Chalmers and O'Farrell, Waters, Macfie, and others have appeared dealing with this subject. Fantham (1915) has studied the organism from a morphological point of view and considers it a distinct species, but this requires confirmation. Dobell, on the other hand, finds no reason for differentiating the spirochæte from the common organisms of the mouth—*Spironema buccale*—and a number of other spirochætes found in wounds and on exposed surfaces.

The pathology is unknown, and further observations on this point are required, in view of the almost universal presence of spirochætes in the sputum, before accepting the hypothesis that this organism is the cause of a special form of bronchitis.

Digitized by Google

CHAPTER X

YELLOW FEVER

Synonyms.—Typhus Icteroides; Fiebre Amarilla (Spanish).

Definition. — An acute, specific, febrile disease probably caused by *Leptospira icteroides* of Noguchi, occurring epidemically, or as an endemic, within a peculiarly limited geographical area. Though subject to great variations, its typical clinical manifestation may be said to be characterized by a definite course consisting of an initial stage of sthenic nature, rapidly followed by an adynamic condition in which such evidences of blood destruction as black vomit, albuminuria, and hæmatogenous jaundice are liable to occur. One attack generally confers permanent immunity. The *Leptospira icteroides* is transmitted by the domestic mosquito, *Stegomyia fasciata* (*S. calopus*).

Geographical distribution.—Of all the important zymotic diseases, yellow fever has the most restricted geographical range. Its centre is the West Indies, spreading north to the United States and Mexico; south to the Brazils and, at times, as far as Buenos Ayres and Monte Video; west to Central America, and across the Isthmus of Panama to the Pacific coast, along which it extends north to the Gulf of California and south to Guayaquil. It appears to be endemic on the West Coast of Africa.

Yellow fever has been imported frequently into Portugal and Spain and Italy. Although a good many died in these visitations, the disease has never obtained a permanent footing in Europe. Cases have occurred in seaport towns in France and Great Britain —Brest and Swansea, for example; invariably, however, these little epidemics have died out.

In several of the West India Islands yellow fever is endemic. Until recently it was always to be found in Havana. Formerly the Brazils enjoyed an absolute immunity; but from 1849, when yellow fever was introduced for the first time into Bahia by a ship from New Orleans, it was practically endemic in the large cities until the institution of anti-stegomyia measures. At Rio de Janeiro sporadic cases occurred till quite recently, and it is still common in Manaos. In such places as New Orleans, Charleston, Monte Video, and Buenos Ayres, although now and again epidemics

Digitized by Google

of great severity broke out, several years have now passed without its appearing. Some of these epidemic visitations have brought a heavy death-bill: thus, in New Orleans, in 1853, 7,970 people died of yellow fever; in 1867, 3,093. In Rio, in 1850, it claimed 4,160 victims; in 1852, 1,943; and in 1886, 1,397. In Havana the annual mortality from this cause used to range from 500 to 1,600 or over, but now apparently it has been stamped out.

Epidemiology. *Influence of atmospheric temperature.* — The histories of these and other epidemics show that the virus of yellow fever can be transported from one place to another, and that for its development in epidemic form it requires a mean atmospheric temperature of over 75° F. (24–25° C.), which is the optimum temperature for growth of the *Leptospira icteroides.* It ceases to spread when the thermometer sinks below this point, and it stops abruptly as an epidemic when the freezing-point is reached. Dampness favours yellow fever; it is therefore most prone to occur and to spread during the rainy season.

Usually a seacoast disease.—The favourite haunts of the disease are the seacoast towns, the banks of rivers, and flat delta country. Rarely does it pass far inland or ascend high ground. Still, there have been exceptions to this general rule; for yellow fever has been found far inland, and at a considerable elevation (São Paulo, Brazil, 2,500 feet; Newcastle, Jamaica, 3,000–4,000 feet). Villages are seldom affected; nor does the disease readily spread if introduced into rural localities. In spreading inland it follows the lines of communication—railways, canals, navigable rivers.

A ship disease.—Ship epidemics were common occurrences formerly. The ideal haunts of yellow fever are the low-lying, hot, squalid, insanitary districts in the neighbourhood of the wharfs and docks of large seaport towns.

A place disease.—It is, in a sense, a place disease like malaria. That is to say, if the patient be removed to a hitherto unaffected spot, his attendants and neighbours will not contract the disease unless the spot itself first become infected. The occurrence of this place infection will depend on whether the particular locality affords in sufficient numbers the appropriate intermediary—the stegomyia mosquito—for the transmission of the germ brought by the patient. It is safe, therefore, to visit a yellow-fever patient if he is lodged outside the endemic or epidemic area; but it is never safe for the susceptible to visit the endemic area, whether they come into direct contact with the sick or not.

Digitized by Google

Immunity acquired by prolonged residence or by a previous attack.—A well-established fact about yellow fever is that the natives of, and those who have lived for a long time in, the endemic area are practically immune from the disease; or, if they are attacked, the disease is usually of a very mild type. It is also said that if the native quits the endemic area his immunity decreases in proportion to the length of time he remains away; so that, after long absence, on his return to the endemic area he may be attacked just as an ordinary visitor might be.

Race as influencing susceptibility.—Formerly it was believed that the negro is little liable to yellow fever, and that when he gets it the attack is usually mild; and also that the yellow-skinned races are more susceptible than the negro, but less so than the European. The facts on which this belief was founded may admit of another and more rational explanation than that of varying degrees of racial susceptibility. Relative racial susceptibility may be more a matter of racial opportunity than of colour of skin; the negro from a non-endemic place—Barbadoes, for example—is just as liable as the European to an attack of yellow fever should he visit an endemic or epidemic area.

Incubation period.—Precise experiments indicate that the incubation period of yellow fever rarely exceeds four or five, with a limit of thirteen days; it may, it is said, be much shorter. The extreme limits are one to fifteen days in the temperate zones, one to thirty days in the tropics. Occasionally it happens that the disease breaks out in a ship after she has been several weeks at sea, having had no communication with the land or with another ship in the meantime. The rationale of this is that infected mosquitoes may have been in the ship from the time she left port, but the crew may not have been bitten and thus infected until long afterwards.

Incubation period preceding epidemic extension.—It has been observed that a period of at least a fortnight elapses between the arrival of a yellow-fever patient in a hitherto uninfected district and the occurrence of the first case of the epidemic he may give rise to. That is to say, that although, as stated above, the incubation period of yellow fever—the period elapsing between the introduction of the virus into the body and the on-coming of fever—is usually only from three to five days, yet a period of at least twelve days must elapse before that virus, after removal from one human body, can be effectively implanted in another human body, which is the period required for the cycle of the leptospira to take place in stegomyia.

Digitized by Google

Duration of the infective period.—This is singularly brief. A yellow-fever patient is dangerous to his neighbours only during the first three or four days of the disease. After this he cannot confer infection.

Etiology.—A great many attempts have been made in the past to discover the germ or virus of yellow fever, and a corresponding variety of organisms have been described. At last Noguchi claims to have dispelled all doubts by his work in Guayaquil in 1918. He found that guinea-pigs injected intraperitoneally with a considerable amount (5 c.c. or more) of blood from yellow-fever cases developed a train of symptoms comparable to those occurring in man. By the dark-ground illumination method, considerable numbers of a delicate spirochæte, the *Leptospira icteroides* (Fig. 64),

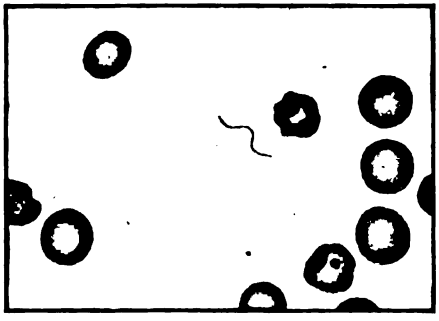


Fig. 64.—Leptospira icteroides in blood of experimentally-infected guinea-pig. × 600.
(After Noguchi, in "Journ. Exp. Med.")

an organism close'y allied to *L. icterohæmorrhagiæ*, were found in the blood, liver, and kidneys; further, he was able to obtain a pure culture of the organism in artificial media and to transmit it through a series of guinea-pigs, and subsequently was able to recover it in pure culture from their organs. Different strains of the organism vary greatly in virulence: some are only feebly pathogenic to guinea-pigs; the majority of the animals employed escaped a fatal infection. The marmoset, like the guinea-pig, also an inhabitant of South America —a significant fact from the epidemiological point of view— is susceptible; on the other hand, a number of other mammalia, including monkeys, rabbits, cats, and sloths, are refractory, as are also birds and reptiles.

The organism grows best, as in the case of *L. icterohæmorrhagiæ*, under aerobic conditions without excessive supply of oxygen in

Digitized by Google

solid media* containing blood-serum (human, sheep, horse, rabbit, etc.). It grows well at a temperature of about 25–26° C., and more quickly at 33° C., multiplying by transverse fission, but it is very sensitive to the presence of bacteria, and is rapidly destroyed when they are present. It is an extremely delicate filament, 4–9 μ in length by 0·2 μ in breadth. The entire filament is not smooth, but is minutely twisted at short and regular intervals, the length of each section being 0·25 μ. In culture it breaks up into a number of refractile granules, and in this form can pass through Berkefeld filters V and N. The possibility of a similar granular phase occurring in the human body must not be lost sight of. The organism is somewhat smaller than the strains of *L. icterohæmorrhagiæ* studied by Noguchi; in other respects it greatly resembles that organism and is actively motile, but can be differentiated by immune serums prepared by Noguchi from guinea-pigs. It is difficult to stain, but can be demonstrated by osmic acid fixation and subsequent staining with Giemsa. The details of its structure are not so accurately made out when stained by Fontana's method, or by carbolized gentian violet, 1 per cent. tannic acid being used as a mordant.

The virulence of some strains of this organism is so great that 0·0001 c.c. of the culture is sufficient to induce fatal symptoms in a guinea-pig. The organism is killed within ten minutes at 55° C. and by desiccation or freezing. Bile and bile-salts dissolve it in certain concentrations, but saponin has no effect; it is readily killed by 2-per-cent. phenol or 0·1-per-cent. bichloride of mercury.

The organism is very scanty in the blood of yellow-fever patients; Noguchi relates that he identified it with certainty, under the dark-ground illumination, in three only out of twenty-seven cases. It would appear to be nowhere abundant in the human body, and Noguchi has found it but once in an emulsion of the liver of a patient who succumbed on the fourth day of the disease. In no case has the organism been found in the urine. In guinea-pigs the organisms enter the bloodstream within forty-eight hours after inoculation; they are most abundant on the sixth and seventh days, and can

* The best medium consists of one part rabbit's serum to three parts of Ringer's solution, used in a combination of a liquid form and a form made semi-solid by adding melted neutral agar (0·3 per cent.). the liquid half of the medium (8 c.c.) being superimposed on the semi-solid half (8 c.c.) in a tall culture-tube. The inoculation of the medium is effected by mixing 1 c.c. of citrated yellow-fever blood with the lower, semi-solid portion of the medium while the latter is still in the fluid state (42° C.). The mixture is then allowed to solidify by cooling, after which the fluid serum-Ringer dilution is poured on to the semi-solid portion, and 1 c.c. more of the same blood introduced. A layer of liquid paraffin is then added. Growth takes place in three to five days. Noguchi succeeded in obtaining only three successful isolations from eleven cases of yellow fever.

Digitized by Google

then be demonstrated in numbers in the liver and kidneys, but become scanty, or completely disappear, before the death of the animal.

Nature of the yellow-fever germ indicated by epidemiology.—In earlier editions of this book Manson foreshadowed the remarkable life-history of *L. icteroides* by pointing out the restricted geographical distribution of yellow fever and the probability of the hypothetical germ (as it then was) having to pass parts of its life-history in an extracorporeal state or medium. These remarks, suggested by the peculiar epidemiological features of yellow fever, received remarkable confirmation from the brilliant work of Reed, Carroll, Agramonte, and Guiteras, and many subsequent workers.

Proof that the virus occurs in the blood.—By injecting blood from yellow-fever cases into six non-immunes, Reed, Carroll, and Agramonte reproduced the disease in five of them within the recognized incubation period. They further demonstrated the infectivity of the blood-plasma and the destruction of the virus at 55° C. From the fact that the virus could pass through a Berkefeld filter they inferred that the hypothetical germ (as it then was) was ultramicroscopic, at least in one stage of its existence—an inference which we now know from the recent work of Noguchi to be correct.

The mosquito the intermediary and diffusing agent of the germ of yellow fever.—Influenced by a number of direct observations and by a long series of carefully conducted culture experiments on the blood, and encouraged by the discoveries in the etiology of malaria which had but recently been made, the American observers thought that possibly, as in malaria, the mosquito was an essential factor in the life-cycle of the yellow-fever germ, as Finlay had conjectured many years before. They then succeeded in transmitting yellow fever to normal persons in a large proportion (83·3 per cent.) of their experiments by means of the common mosquito *Stegomyia fasciata*, an observation since abundantly confirmed. Unfortunately Lazear, one of the courageous band, succumbed to the disease.

The germ not transferable by recently infected mosquitoes.—As might have been expected from the blood-inoculation experiments, it was found that only mosquitoes that had fed during the first three days of the fever were infective, that a developmental process lasting twelve days was necessary before the experimental insects could convey infection, and that they retained their infective power for at least fifty-seven days.

These experiments explained—(1) The impunity with which a yellow-fever patient can be visited by a non-immune if outside

Digitized by Google

the endemic area; the mosquitoes in the vicinity are not infective. (2) The danger of visiting the endemic area, especially at night; the mosquitoes there are infective and active. (3) The discrepancy between the incubation period, three to five days, of the disease, and the incubation period, fourteen days and over, of an epidemic; the necessary evolution of the germ in the mosquitoes infected by the original introducing patient demanding the space of time indicated by the difference between these two periods. (4) The clinging of yellow-fever infection to ships, buildings, and localities; the persistence of the germ in infected mosquitoes (*Stegomyia fasciata*) which are known to be capable of surviving for five months, and probably longer, after feeding on blood. (5) The high atmospheric temperature required for the epidemic extension of yellow fever; such temperature favours the activities and propagation of the mosquito, and is probably also necessary for the evolution of the germ in the mosquito.

As regards *S. fasciata*, the same observers note that to lay eggs she must first have a feed of blood, and that her eggs are deposited about three days after she has so fed. Before the first egg-laying, *S. fasciata* is both diurnal and nocturnal in her feeding habits, biting at any time; subsequently she is strictly nocturnal in this respect. Therefore a stegomyia that bites during the day does not convey yellow fever. She is too young; any parasite she may harbour is immature. In this way is to be explained the impunity with which a yellow-fever centre may be visited during the day, although the visitor may be bitten by stegomyia. Formerly Europeans who lived at Petropolis, a suburb of Rio de Janeiro, and were in the habit of visiting and transacting their business in the low-lying yellow-fever-haunted districts of the city, never contracted the disease unless they were so imprudent as to pass the night in the latter. There is no proof at present that the stegomyia is able to transmit the infection through her ova to the larval mosquitoes.

The parallelism between the etiology of yellow fever and that of malaria is very complete; further, as several species of mosquito of the sub-family Anophelinæ have been shown to foster the malaria parasite, it is not improbable that several species of the genus *Stegomyia* may turn out to be effective intermediaries for the leptospira of yellow fever, such as *S. africana*, *S. argenta-punctata*, and *S. sugens*.

The classical work of the pioneers of the etiology of yellow fever has now been clinched by the discoveries of Noguchi, who has succeeded in transmitting the *Leptospira icteroides* from a

Digitized by Google

stricken to a non-immune guinea-pig after an incubation period within the body of the insect of eight days; this is a shorter period than that enunciated for the human disease, which had been estimated at twelve days, possibly owing to the fact that the leptospira is more abundant in the bloodstream of these animals, and therefore more rapidly undergoes its cycle of development when ingested by the mosquito. It appears that under natural conditions the percentage of mosquitoes which become infected with yellow fever is very small; this is explained by the small quantity (0·01 c.c.) of blood imbibed by a female *Stegomyia fasciata*, whereas 0·1 to 2 c.c. are required to convey the disease to a non-immune person by direct inoculation. Together with this, it is necessary to remember that one infected mosquito means many yellow-fever victims, and that the life of such an insect is usually longer than that of the persons it infects. Noguchi also succeeded in conveying the disease from yellow-fever patients to normal guinea-pigs by means of these insects. Although numerous attempts were made, only three were successful. The exact stages of the life-history of the leptospira within the intermediary host have not yet been traced; but Noguchi notes that the blood-serum and the comparatively aseptic conditions within the mosquito's stomach are such as would favour the multiplication of the organism. It has been proved that the organism can penetrate the intact human skin, and therefore it is not difficult to explain the manner in which the leptospira gains entrance to the tissues of a man who has been bitten by an infective stegomyia. Another interesting fact with reference to the extrinsic life of the leptospira is that it can multiply steadily in a temperature of 18 to 37° C., the optimum being 26° C., a temperature which is found in most tropical countries and certainly in those localities in which yellow fever is endemic.

Symptoms.—There is the same variety in the initial symptoms of yellow fever as in other specific fevers. There may be sudden rigor supervening in the midst of apparent health; there may be only slight chills; or there may be a period of premonitory malaise leading up to the more pronounced symptoms. When fairly started, the procession of events is rapid. The incubation period is from three to six days.

Roughly speaking, and provided there are no complications, an attack of yellow fever is divisible into three stages—(1) the initial fever; (2) "the period of calm," as it is called; and (3), in severe cases, the period of reaction.

The initial fever is usually sudden in onset and lasts from three

Digitized by Google

to four days. The maximum temperature is generally attained within the first twenty-four hours, or by the second day, and, in a case of medium severity, may rise to about 103° or 104° F. During the three or four succeeding days the mercury slowly sinks to 98° or 99°, the daily fluctuations being seldom more than a half to one degree. It occasionally happens that high temperature is maintained for two or three days, and also that the maximum is not attained till the third day; as a rule the thermometer behaves as described, the maximum being reached within a few hours of the onset of the disease. (Chart 9.)

With or soon after the initial chill or rigor, severe headache sets in, and is generally a prominent feature. For the most part the pain is concentrated about the forehead, in the circumorbital region,

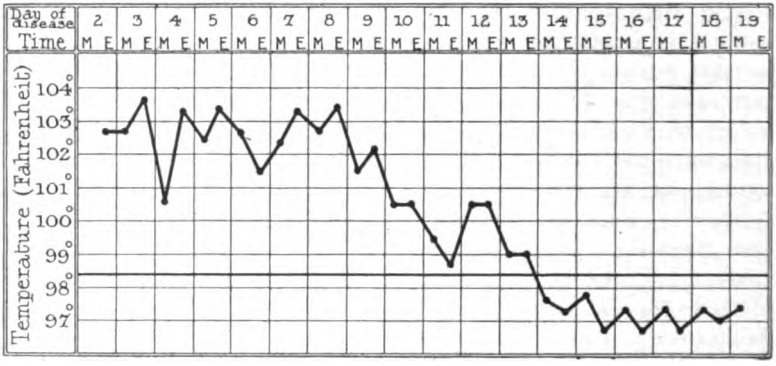

Day of disease
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Time
M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E
Temperature (Fahrenheit)
104°
103°
102°
101°
100°
99°
98°
97°

Chart 9.—Yellow fever. (*After Noguchi.*)

and in the eyeballs themselves. In many cases it is associated with intolerance of light.

Loin pain is another very distressing symptom; it may amount to positive agony. The legs, too, ache excessively—particularly the calves, knees, and ankles; they feel as if broken. Epigastric pain is generally a prominent symptom.

The face is flushed and swollen; the eyes are shining, injected, and ferrety; the skin is dry.

What with pain and febrile distress, the patient rapidly passes into a very miserable condition. He is restless and continually tossing about.

At first the pulse ranges from 100 to 120, and is full and strong; but as the disease progresses the pulse loses its sthenic character, gradually falling in force and frequency until, at the "period of calm," it becomes remarkably slow and compressible, beating

Digitized by Google

perhaps only 30 or 40 times per minute. This fact is of particular value in diagnosis, and is known as *Faget's law*, that is, a falling pulse-rate with a constant temperature, or a constant pulse-rate with a rising one.

At the outset the tongue is not very dirty, but it soon acquires a white coating on the dorsum, the edges remaining clean. It is not so swollen and flabby as in malarial fever; on the contrary, it is rather small and pointed throughout the disease. This is regarded as an important diagnostic mark; taken along with the progressive diminution in the strength and frequency of the pulse, and the peculiar behaviour of the temperature, it is nearly conclusive as to the disease being yellow fever. Later, the tongue dries, and, at the same time, thirst becomes intolerable. The palate is congested and swollen; the gums may also swell and bleed.

The congested appearance of the face at the onset of the disease tends to subside; so that by the time the asthenic stage is reached the features may have become shrunken and small, the eyes sunken, and the eyelids discoloured by ecchymoses.

In some cases the skin is hot and dry throughout; in others it may be bedewed with perspiration from time to time; or the sweating may be constant, especially so if collapse sets in.

By the third day the scleræ assume a yellowish tinge, and very often the skin acquires the yellow colour from which the disease derives its name. It must not be understood, however, that every case presents this colour of skin; in some it is entirely absent, but if carefully looked for there is always some yellowness of the scleræ to be discovered. The yellow tinging of the skin generally shows about the end of the first stage, deepening in intensity as the case advances, and remaining apparent for a considerable time after convalescence has become established. It ranges in depth from a light saffron tint to a deep mahogany brown. In fatal cases it is always present—not necessarily during life, but invariably after death. The skin in bad cases is said to emit a peculiar odour like gun washings, or, as Jackson puts it, like the smell of a fish market.

Petechial, erythematous, papular, and other eruptions may show themselves in different cases; but in yellow fever there is no characteristic eruption, unless it be an erythematous congestion of scrotum or vulva, which occurs in a proportion of cases and is said to be diagnostic.

An important feature, from the diagnostic as well as from the prognostic point of view, is the appearance, in some cases almost from the outset of the disease, of albumen in the urine, together

Digitized by Google

with a tendency to suppression. In mild cases these features may be little marked; but in severe cases, particularly during the stage of depression, the urine may fall to a few ounces, and be loaded with albumen to the extent of one-half or even two-thirds. The more pronounced these symptoms, the graver is the prognosis. Urea (even during the incubation period) and uric acid are very much diminished, the former in severe cases falling to 1·5 grm. to the litre. The urine is almost invariably acid, depositing granular casts, and giving spectroscopic evidence of hæmoglobin. Bile pigments show themselves towards the end of the disease; their appearance is regarded as a favourable omen. Hæmorrhage from kidneys or urinary tract is not uncommon.

Delirium may occur, but is not an invariable feature. Usually, after the initial stage of restlessness and acute suffering, the patient becomes torpid, and perhaps taciturn. In bad cases coma, subsultus, etc., may gradually supervene, the temperature rising as death approaches and even after death.

At the outset the bowels are confined. In the second stage diarrhœa, perhaps of black material resembling the vomit (*see* below), may supervene; or there may be actual hæmorrhage of bright-red blood from the bowel.

The well-known *black vomit*—always a grave symptom, but fortunately not by any means an invariable one—forms one of the most striking features of this disease. In the earlier stages of the fever, vomiting of bilious matters is a common occurrence. This may subside, or, after a time, give place to a coffee-ground vomit which seems to gush up without straining or effort on the patient's part, and which gradually deepens in colour until it becomes uniformly black. On microscopical examination the vomited material is found to consist of broken-down blood-corpuscles and altered hæmoglobin suspended in a yellowish mucoid fluid. This material is, doubtless, in the main derived from blood transuded through the walls of the capillaries of the mucous membrane of the stomach. It is intensely acid. Though the black vomit may not always be seen in fatal cases during life, it is invariably found in the stomach on post-mortem examination.

Sometimes pure blood is thrown up from the stomach; similar passive hæmorrhages may take place from almost any part of the body—from eyes, ears, nose, mouth, bladder, uterus, and so on.

Death may occur during the early acute stage, being preceded by a rapid rise of temperature. The majority of deaths occur on the fifth and sixth days; the end seldom comes before the third

Digitized by Google

or after the eleventh day of the disease. It is generally preceded by a rapid fall of temperature.

In mild cases the "period of calm," which sets in after the subsidence of the initial fever, may last for several days before convalescence is established. In such, recovery once begun is usually very rapid; in a week from the beginning of the disease the patient may be about again. In severe cases, however, the period of calm is followed by a third stage, the stage of reaction, in which the temperature again rises, though not to so high a point as in the initial fever, and a sort of remitting fever of an adynamic type keeps on for several days or weeks. This secondary fever is more prolonged if there is any complication, such as abscess, boils, parotitis, buboes, hepatitis, and so forth. The icterus is now very pronounced; black vomit may recur, or appear for the first time; perhaps a profuse diarrhœa ends in collapse; or the urine may be suppressed, stupor, coma, and other nervous symptoms ensuing, and very often ending in death. In other instances the secondary fever terminates in a crisis of sweating and a prolonged convalescence.

Relapse may occur at any time up to two or three weeks after the subsidence of the initial fever. It is specially prone to occur if the patient has been guilty of any dietetic imprudence during the period of calm—a period at which the appetite may return to some extent. Relapses are very dangerous.

As a rule, there is a slight leucocytosis early in the disease, soon followed by a leucopenia; the polymorphonuclear cells predominate. The serum, according to Noguchi, shows marked immunity reactions to the *Leptospira icteroides*, thus strengthening the evidence that this organism is the cause of the disease. A positive Pfeiffer reaction can also be obtained by injecting culture of the leptospira together with the serum of convalescent yellow-fever cases into the abdominal cavity of a guinea-pig.

Prognosis and mortality.—Prolonged initial rigors, algidity, convulsions, suppression of urine, coma, hæmorrhages, are all unfavourable symptoms. The prognosis is good if the temperature during the initial fever does not exceed 103° to 105° F. It is better for women (although, if pregnant, abortion is almost invariable) and children than for men; better for old residents than for new-comers; worst of all for the intemperate. According to a table given by Sternberg, of 269 carefully observed cases there were no deaths in 44 in which the temperature did not rise over 103°; per contra, in 22 cases in which the thermometer rose over 106° there were no recoveries. The mean mortality in

Digitized by Google

the whole 269 cases was 27·7 per cent. In some epidemics it has risen as high as 50 or even 80 per cent. of those attacked, but the foregoing may be taken as a fairly representative mortality in yellow fever among the unacclimatized—something between 25 and 30 per cent. Among the permanent inhabitants of the endemic districts the case mortality is very much lower—7 to 10 per cent. During epidemics abortive and ambulatory cases occur; in these, icterus and other characteristic symptoms are often absent. Such cases may be hard to diagnose from febricula or mild malarial attacks. In them the mortality is nil. Some epidemics are particularly mild; in others the majority of the patients die. In the same epidemic the cases may vary in severity from time to time. In children the mortality is insignificant.

Pathological anatomy.—Depending probably on hæmoglobin diffused in the liquor sanguinis and tissues, and not on biliary pigment, the yellow colour of the skin is most marked in the dependent parts of the cadaver, especially in those parts which are subjected to pressure. Rigor mortis is pronounced. Petechiæ are common in the skin and serous membranes; more considerable extravasations of blood may be found in the muscles. The brain and meninges are hyperæmic, and may be studded with minute hæmorrhagic effusions; like the other tissues of the body, they may be stained a lighter or deeper yellow. The cartilages are intensely yellow. The blood in the vessels of the general circulation is not firmly coagulated. The blood-corpuscles appear to be normal, although there can be little doubt that there is in this disease a liberation of hæmoglobin, arising, possibly, from destruction of a proportion of the corpuscles. An important fact, as explaining the liability to passive hæmorrhages, is the existence of a generalized fatty degeneration of the capillaries and smaller blood-vessels. The stomach, as stated, always contains more or less black material, sometimes fluid blood, such as may have been vomited during life. The folds of the gastric mucosa are swollen; here and there are arborescent patches of congestion, and ecchymoses. Observers are not agreed as to the nature of this congestion—whether it is passive or inflammatory. The small intestine may contain a dark, acid material similar to that in the stomach, and doubtless coming from the same source. Like that of the stomach, the mucous membrane of the intestine shows patchy arborescent injection.

As compared with other fevers, in yellow fever the liver is characteristically affected. As a rule, if death has occurred at the later stages, this organ is somewhat exsanguine, friable, and presents a yellowish colour from profound fatty changes in the cells. Occa-

Digitized by Google

sionally, though rarely, it may be hyperæmic and dark; more usually it is brownish-red or saffron-coloured. Throughout the gland the cells—particularly those about the periphery of the lobules—on microscopic examination are found to be necrotic and studded with extravasated blood. The nuclei in some instances, as well as the protoplasm of the cells, show fatty changes; the latter may be completely disintegrated. In the great majority of cases this fatty degeneration is well marked. It is not confined to the liver; every organ of the body is more or less affected in the same way.

The spleen is not characteristically affected, but the kidneys show signs of parenchymatous nephritis. Hæmorrhagic foci under the capsule and in the cortex are common. The renal epithelium shows cloudy swelling passing on to fatty degeneration and desquamation. The tubules, here and there, are filled with infarcts, either of an albuminoid material or of débris of desquamated epithelium, corresponding with the numerous casts which can be discovered in the albuminous urine.

Diagnosis.—Practically the only diseases with which severe yellow fever is likely to be confounded are *bilious remittent, infectious jaundice*, and *blackwater fever*. The difficulties of diagnosis on clinical grounds are often great, particularly in the earlier cases of an epidemic. When several deaths, preceded by fever and black vomit, have occurred within a limited area and in quick succession, a suspicion of yellow fever becomes a certainty. There is no clinical feature, so far as is known, which would distinguish a mild attack of yellow fever from an ordinary febricula, nor any pathognomonic clinical sign that would absolutely distinguish a malarial remittent from yellow fever. *Dengue* is probably one of the most difficult diseases to differentiate from mild yellow fever. The facies, orbital pains, and backache are similar to those of dengue, but the appearance of the characteristic eruption of the latter disease on the fourth day should settle the diagnosis in any doubtful isolated case. Probabilities must be weighed in diagnosis when it is based on clinical grounds alone. The only reliable guides are the discovery of the malaria parasite and the characteristic pigment and leucocytic variation in malarial fever, and the determination of their absence in yellow fever; and, when cases come to the post-mortem table, the presence of pigment in the viscera in the former, and of extensive fatty degeneration of the liver cells in the latter. Occasionally both diseases may coexist.

Noguchi's recent researches suggest that an agglutination test

Digitized by Google

may soon be employed in practice, for the serums of yellow-fever patients agglutinate cultures of the *Leptospira icteroides* in high dilutions. Complement-deviation tests have so far proved less satisfactory. The diagnosis of yellow fever from malarial and blackwater fevers is more fully considered on pp. 64, 106.

Treatment.—Formerly a much more active treatment than that in vogue at the present day was the fashion for yellow fever. It is now recognized that, as with most specific fevers, the treatment is more a matter of nursing than of drugs.

Experience has shown that a smart purgative at the very onset of the disease is beneficial. With many castor oil is the favourite drug, but to be of service it has to be given in very large doses—2 to 4 oz. Others use calomel; or calomel combined with quinine—20 gr. of each. Others, again, prefer a saline. The purgative, whichever be selected, must not be repeated, nor, for that matter, given at all if the patient is not seen until after the second day of the disease.

Hot mustard pediluvia, frequently repeated during the first twenty-four hours, the patient and bath being enveloped in a blanket, are much in favour. They are said to relieve the cerebral congestion and the intense headache. Very hot baths, with subsequent blanketing and sinapisms to the epigastrium, are also said to have a similarly favourable influence on the congestion of the stomach which is, undoubtedly, another constant feature of the disease. For high fever, antipyretic drugs, cold baths, iced injections, cold sponging, and the like may be carefully employed. In view of the asthenic nature of the disease, the less depressing measures should be preferred.

Vomiting may be treated with sinapisms and ice pills, or with small doses of cocaine. Morphia is dangerous and must be avoided. For black vomit, frequently repeated doses of perchloride of iron, ergotine injections, acetate of lead, and other styptics have been recommended. For restlessness, phenacetin or antipyrin is used. When the skin is dry, the urine scanty, and the loins ache excessively, Sternberg recommends pilocarpine.

After the fourth or fifth day the flagging circulation demands stimulants of some sort. Iced champagne, hock, or teaspoonful doses of brandy given every half-hour may tide the patient over the period of collapse. Great care, however, should be exercised in the use of these things; if they seem to increase the vomiting and the irritability of the stomach, they must be stopped at once.

The feeding is an important matter. So long as there is fever the patient has no appetite; during this time—that is, for the first

Digitized by Google

two or three days—he is better without food. When the fever subsides, appetite may return, and a craving for nourishment become more or less urgent; the greatest care, however, must be exercised about gratifying this untimely appetite. Only the blandest foods, and these only in very small quantities, should be allowed—such as spoonfuls of iced milk or chicken tea. Gradually the quantities may be increased; but, even when convalescence is established, solid food must be partaken of very sparingly, and it must be of the simplest and most digestible description. Indiscretion in eating is a fruitful cause of relapse in yellow fever; and it must be borne in mind that in this disease relapse is exceedingly dangerous. Nutrition may be aided by nutrient enemata.

The Sternberg treatment.—Sternberg introduced a system of treatment by alkalis which promises well. It is directed principally to counteracting the hyperacidity of the gastric and intestinal contents—always a marked feature in yellow fever. His prescription is 150 gr. of sodium bicarbonate and $\frac{1}{3}$ gr. of mercury perchloride in a quart of water; of this $1\frac{1}{2}$ oz. is given every hour. This, he claims, not only neutralizes the acidity of the intestinal contents but increases the flow of urine, the perchloride of mercury tending to check fermentation changes in the alimentary canal. Of 301 whites treated in this way only 7·3 per cent. died, and of 72 blacks all recovered. Other encouraging figures have been adduced as to the efficacy of this line of treatment, which is certainly deserving of further and more extended trial.

Serum treatment.—A polyvalent immune serum has been prepared, as announced by Noguchi in a recent communication, and indicates that in future such a method will be employed in the treatment of yellow fever. When administered to guinea-pigs within the first 96 hours, in successive doses of 0·01, 0·1, and 1 c.c., it is capable of completely preventing the development of the disease. Employed at a later stage, when jaundice and nephritis have been present for several days, the serum has no perceptible beneficial effect. It is prepared from the horse by injecting into the jugular vein gradually increasing amounts of rich, live cultures of *Leptospira icteroides*. Such a serum rapidly agglutinates the organism.

Prophylaxis.—It is the duty of sanitary authorities in tropical countries, so far as possible, to free of mosquitoes the areas over which they have charge. If this were done everywhere there would be no malaria, no filariasis, no dengue, and no yellow fever. Although complete extermination is not to be expected, relative extermination of mosquitoes is worth attempting, and certainly

Digitized by Google

much can be attained in this direction by the vigorous use of the now well-known measures. In Havana, by such means, in a very few months the number of mosquitoes was reduced 90 per cent., with a corresponding gain to the community in the diminution of mosquito-conveyed disease. The same has happened in Panama, Rio, and elsewhere.

During epidemic visitations or during exacerbations of endemic yellow fever, non-immunes should, if possible, immediately quit the implicated locality. Above all, the slums and low-lying districts of the town should be shunned. These places should not even be visited; or, if visits have to be made to them, they should be as brief as possible, and not made after sundown. The susceptible should not sleep in the lower storeys of houses, and should pay great attention to general health, carefully avoiding all causes of physiological depression or disturbance. Sailors must not be allowed on shore.

All water-tanks and cisterns must be effectually screened by fine-meshed metallic gauze against the stegomyia mosquito; all puddles and stagnant water abolished; all cases of any kind of fever, no matter how mild they may be or what their nature, must be reported at once to the central sanitary authorities, who should have full powers promptly to screen or otherwise deal with them and the houses in which they are. The general use of mosquito-nets must be insisted upon.

Any delay in recognizing the earliest cases of a threatened epidemic is, as shown by experience in New Orleans, most dangerous, leading, as it may, to the rapid multiplication of infected centres.

Ships should not be allowed to clear from infected ports, nor to enter non-infected ports, during the warm season, without adequate inspection. If, on entering port, yellow fever is found on board, the cases should be isolated in a quarantine hospital where there are no stegomyia mosquitoes, the ship thoroughly cleared of mosquitoes, and the passengers and crew prevented for at least five (better thirteen) days from communicating with the shore, or until every risk of conveying infection has passed away. Steamers trading on the Amazon have now been made relatively mosquito-proof by means of wire-gauze netting fitted to the windows and doors.

Should the disease appear in a locality which is not habitually a yellow-fever centre, and of which the population is small, an economical plan of dealing with the threatened danger is for the authorities promptly to remove the entire population of the neighbourhood, with the exception of the insusceptible and those

Digitized by Google

in attendance on the sick, and to place the deported population, before dispersion, in a thirteen days' quarantine camp. Meanwhile the infected area must be rigidly isolated and its mosquitoes destroyed. In this way the spread of the disease will be prevented.

In the event of yellow fever breaking out in the crew of a man-of-war, the cases, if possible, should be sent ashore, and the ship hurried north or south into cold weather, any mosquitoes which may have found their way on board being at once destroyed.

In the case of the appearance of yellow fever in a large town, the method which was so successfully adopted by Surgeon-General Gorgas must be adopted. Funds and authority must be obtained at once. An efficient and adequate sanitary staff must be promptly organized and instructed in their duties. Cases of every kind of fever as well as cases of yellow fever should be immediately reported, and the patients promptly protected from mosquito-bite by wire screens. At the same time the systematic destruction of mosquitoes in their breeding-places and in the patients' and neighbouring houses must be rigidly enforced. The infected houses should be carefully sealed up by pasting paper over all the doors, windows, ventilators, chimneys, and cracks, and the fumes of pyrethrum or of burning sulphur—2 lb. per 1,000 cubic feet of space—or other insecticide employed to stupefy the insects, which should afterwards be swept up and burned. In this way, in 1901, yellow fever was stamped out in ninety days in Havana, a city where for a period of 140 years it had held uninterrupted sway. In this way, in 1905, New Orleans was freed from the disease in a much shorter period than in any previous epidemic; and in this way Gorgas made the line of the Panama Canal as healthy as New York. Similar results from similar measures are being obtained in the large Brazilian ports.

Guiteras has shown, in a practical manner, that yellow-fever patients may be admitted to the wards of a general hospital or be nursed in private houses with impunity, provided they are protected by effective mosquito-netting from mosquito-bite during the first three or four days of their illness.

Portability of the virus in fomites and merchandise.—Many instances have been adduced as conclusive evidence of the portability of the virus of yellow fever in fomites. But the very thorough and carefully conducted experiments carried out in Cuba by Drs. Reed, Carroll, and Agramonte go far to prove that fomites have nothing whatever to do with the conduction of the disease. A small, ill-ventilated, badly lighted wooden hut was erected near Havana during the prevalence of epidemic yellow

Digitized by Google

fever. The fresh and stale fomites of yellow-fever patients, in the shape of soiled bedding, clothes, black vomit, etc., were strewn about or stowed away in great profusion in this close hut. and among them, lying on beds that had been occupied recently by yellow-fever patients, wearing these patients' soiled night-clothes and using their soiled blankets, seven non-immunes (that is, white men, recently arrived and never previously affected with yellow fever) slept during, in the aggregate, sixty-three nights—from November 20th, 1900, to January 31st, 1901—with absolute impunity.

Immunity of the native as affected by anti-stegomyia sanitation.—The immunity of the native of the endemic areas of yellow fever is usually attributed to a mild attack in childhood. If yellow fever has been exterminated from Havana and other endemic centres by anti-stegomyia and other measures, the children in these places can no longer be attacked by the disease. It follows that in the course of one generation the entire population will become non-immune. Doubtless sooner or later the germ of yellow fever will be introduced again, and then, having a population entirely non-immune to spread in, unless promptly checked a far more extensive epidemic than ever devastated these places in less scientific days will ensue. This can be confidently predicted if it be true that the present immunity of the native depends on an attack of ordinary yellow fever in childhood. One is inclined to think that this explanation does not cover the entire ground; for, if the disease be so mild in childhood as not to be recognizable, how was it that Gorgas stamped out yellow fever in Havana, and how is it that the disease is not in evidence there now? There may be two strains of yellow-fever virus—one of great virulence, one of little virulence. Specifically the same, they are mutually protective, much in the same way as with vaccinia and small-pox. The immunity of the native and the old resident could be attributed to epidemics or endemics of the mild strain of yellow fever, which, could it be recognized clinically, might be used as a vaccine against the more virulent disease. It is not improbable that one of the indigenous mammals of South America, as for instance the marmoset, which has been found capable of infection, may act as a reservoir of the virus, and that within its body the organism may become attenuated and so less virulent for man.

The production by Noguchi of an artificial immunity in guinea-pigs by means of repeated injections of attenuated cultures of *Leptospira icteroides* holds out a reasonable hope that, in the very near future, killed cultures of this organism will be used as a pro-

Digitized by Google

phylactic injection in man, and may be employed in much the same way as in antityphoid inoculation.

Introduction of yellow fever into Asia.—There is another important matter in connection with this disease which ought without delay to be made a subject for international consideration, namely, the possibility of the spread of yellow fever to Asia, the Eastern Archipelago, Polynesia, and East Africa. It has spread in the past to Europe; this is a comparatively unimportant matter, as the climatic and hygienic conditions in that continent are not favourable to the stegomyia mosquito, and therefore to the extension of the disease. It is otherwise in this respect, it is to be feared, with Asia. Fortunately, yellow fever, so far as known, has never appeared in the crowded, filthy cities of the East; but, should it ever be introduced there, the favourable climatic conditions, the surpassing filth everywhere, the presence of stegomyia mosquitoes, and the too frequent absence of efficient sanitary machinery will enable it to spread like wildfire in an entirely non-immune population. The probable reason of its non-introduction into Asia is that the trade route from the West Indies and Central America to China and India has hitherto not been a direct one, but has passed by a long circuit either to the north or to the south. When the American inter-oceanic canal is in full use there will be direct and rapid communication between the present yellow-fever centres and Asia. With this more direct and more rapid communication there will arise a corresponding risk of spreading yellow fever into a huge section of tropical humanity which has hitherto enjoyed exemption from one of the deadliest diseases that afflict mankind. An infected mosquito (and *Stegomyia fasciata*, according to Giles, is a good traveller), either shipped by accident or brought on board by some thoughtless or malicious person, could easily be conveyed alive to the shores of Asia, and would suffice to set, so to speak, the whole of the tropical section of the Eastern hemisphere in a blaze. The history of the spread of disease by the rapid methods of modern travel is full of examples that should serve as a warning to our rulers and responsible sanitary authorities. Let us hope that this important matter will receive the attention it demands, and that due care will be exercised that America does not reciprocate the introduction of cholera from Asia by a return gift of yellow fever.

Genus Stegomyia

The members of this group of mosquitoes, belonging to the sub-family *Culicinæ*, present very distinctive characters. Their ova, instead of being cemented together to form rafts as in other *Culicinæ*, are deposited separately,

Digitized by Google

each being surrounded by small air-chambers. Their larvæ are somewhat elongate, with rudimentary antennæ and a short stout siphon; they maintain an almost vertical attitude. In the nymphæ the trumpets are expanded and broadly triangular in shape. The imago exhibits a distinctive scale structure and, at all events in early life, in some species observes diurnal habits.

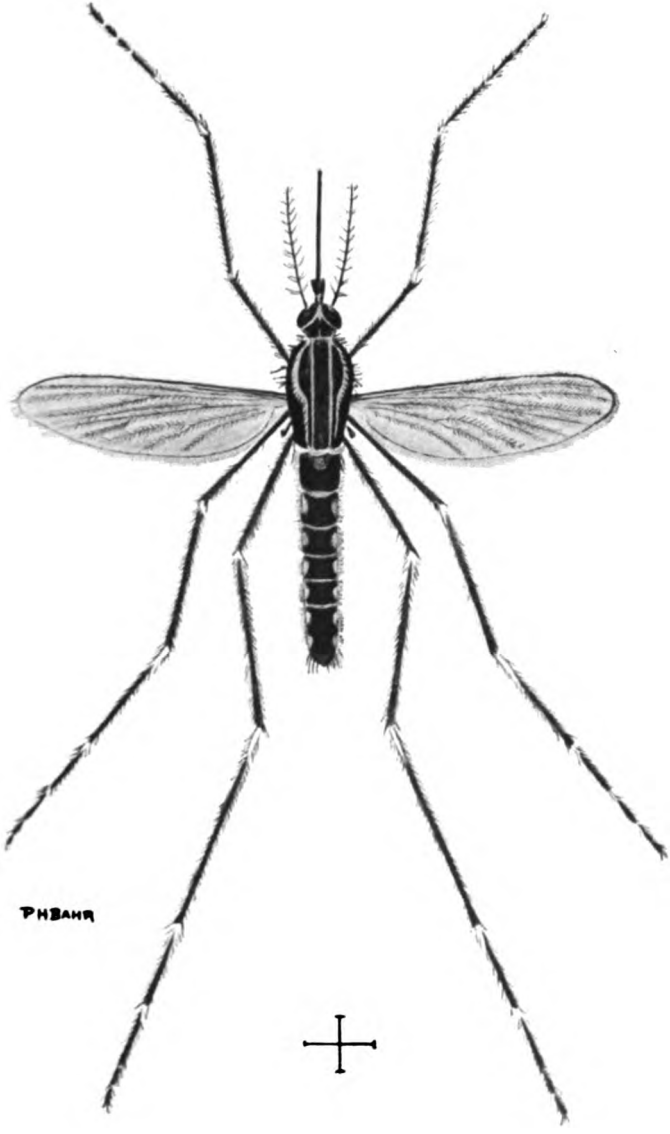
The stegomyiæ are easily recognized by the broad, flat, imbricated scales which completely cover the head and abdomen, and which are invariably present on the middle lobe and frequently also on the lateral lobes of the scutellum. These scales give to the insect a satin-like appearance which is quite characteristic. They are mostly small, black insects, with white, silvery, or yellow lines, bands, or spots on the thorax and legs. In India they are known as "tiger mosquitoes" on account of their striped appearance. They seem to have a decided preference for the littoral, and certain species (*S. fasciata*, *S. scutellaris*) are frequently found on ships and are doubtless distributed by this means. At present the genus *Stegomyia* includes nineteen species, all of which are easily identifiable by reason of their striking thoracic and other ornamentation. Of these the type species, *S. fasciata*, is the most important on account of its wide distribution in all tropical and subtropical countries, and of its share in the propagation of yellow fever.

S. fasciata (Plate XIII.) can be recognized by the peculiar lyre-shaped ornamentation of its thorax, composed of two dull-yellow parallel lines in the middle and a curved silvery line on each side.* The proboscis is not banded; the abdomen is banded basally; the last hind tarsal joints are all white, and some of the other tarsal joints are marked by light bands basally. This widely distributed species is essentially a domestic form, and bites with avidity. It breeds in small artificial collections of water, such as barrels, puddles, cisterns, sagged rain-gutters, and even in such small receptacles as sardine-tins. The nature of the water appears to be a matter of indifference. The eggs resist a considerable degree of desiccation, and, as they may sink to the bottom of the water in which they lie, are readily pumped into the water-tanks of ships.

Although widely distributed, *S. fasciata* does not occur abundantly in certain parts, such as the Malay States, China, and Africa, where its place is taken by closely allied species such as *S. scutellaris* in the Malay States, China, etc., and *S. africana*, *S. argenta punctata*, and others in Africa. It is quite possible that, besides *S. fasciata*, other species belonging to the genus may be able to transmit the germs of yellow fever and dengue, and *Filaria bancrofti*.

* This ornamentation is constant, but the median thoracic stripes are absent in a variety called *S. fasciata mosquito*.

Digitized by Google



STEGOMYIA FASCIATA, ♀.

PLATE XIII.

Digitized by Google

Digitized by Google

CHAPTER XI

INFECTIOUS JAUNDICE

Synonyms. — Icterus Gravis; Spirochætosis Icterohæmorrhagica; Weil's Disease; Mediterranean Yellow Fever; Odau-eki (Japanese).

Definition.—A severe form of fever caused by the *Leptospira icterohæmorrhagiæ*, associated, though not invariably, with jaundice, enlargement of the liver, and sometimes of the spleen. The natural reservoir of infection would appear to be the rat (*Rattus rattus* and *Rattus norvegicus*).

History.—An acute febrile illness associated with jaundice and a high mortality was first described by Weil in 1886, and has been known as Weil's disease. In 1915 Inada, Ido, and other Japanese investigators described the spirochæte *Leptospira icterohæmorrhagiæ* as the cause of the disease. In the early summer of 1916 this disease occurred sporadically among the allied and enemy troops in France, and the Japanese discovery was soon confirmed by Stokes, Ryle, and Tytler among British troops, and by Uhlenruth and Fromme on the German side, while Bonini recognized it on the Italian front. In 1917 the same Japanese investigators proved by means of guinea-pig inoculations the presence of the leptospira in otherwise healthy rats (*R. norvegicus* and *R. alexandrinus*).

Geographical distribution.—The disease appears to be especially prevalent in Japan; during the recent War outbreaks occurred among the troops in Gallipoli and Salonika, and also in Egypt, where the disease has long been known to exist. It is found along the North African coast and the shores of the Mediterranean. It is known to occur in France, Italy, Germany, the United States, Peru, and Brazil, and is endemic in West Africa, where it possibly has been mistaken for yellow fever. The form of the disease, as it occurs in the tropics, is said to be more virulent, though further researches on this point, as well as on its distribution in hot countries, are necessary. In Europe it is said to be more common in summer time.

Etiology.—*L. icterohæmorrhagiæ* is found in the blood, urine, cerebro-spinal fluid, and sputum. It is a spiral filament with wide

Digitized by Google

flexures, the individual spirals being in close apposition (Fig. 65, 1). The largest forms attain a length of 20 μ by 0·25 μ.

The parasites appear to conform to three principal types—(1) a short, thick spirillum with three or four bold curves; (2) nearly straight forms with fine, closely-set spirals; and (3) longer-thread forms curved at one or both ends.

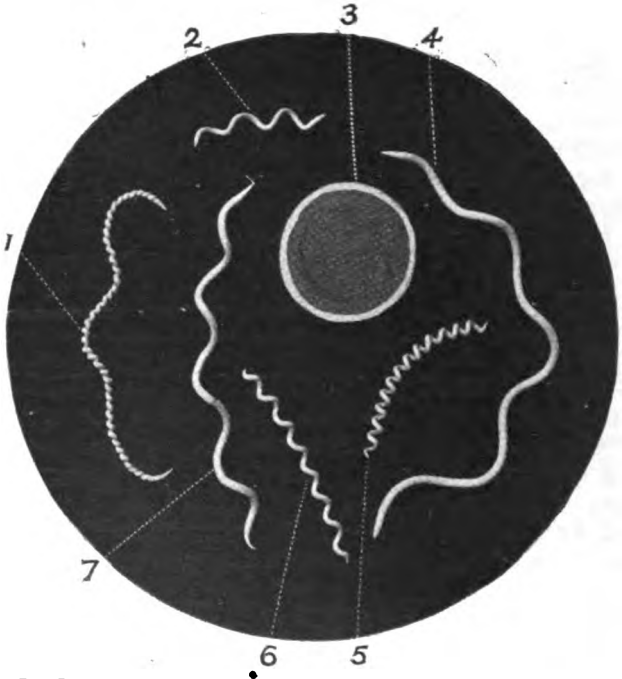


Fig. 65.—Schema of different forms of spirochætes. × 10,000 diam.
(After Dobell; courtesy of Wellcome Bureau Sci. Res.)

1. Leptospira icterohæmorrhagiæ (Inada and Ido) Noguchi. Cause of spirochætal jaundice (Weil's disease).
2. Spironema eurygyratum Werner. Commonly found in human fæces, both in health and in disease (e.g. dysentery).
3. Human red blood-corpuscle on same scale.
4. Spironema recurrentis Leber (= Spirochæta obermeieri Cohn). Occurs in blood in relapsing fever.
5. Spironema pallidum (Schaudinn) Vuillemin (= Spirochæta pallida Schaudinn = Treponema pallidum Schaudinn). Syphilis.
6. Spironema gracile Levaditi and Stanesco (= Treponema colligyrum Noguchi). Found on external genitalia, in health and in various diseased conditions.
7. Spironema refringens Schaudinn (emend.) (= Spirochæta refringens Schaudinn). Occurs in syphilitic lesions on external genitalia.

Frequently it is not possible to detect very fine spirillation either by the dark-ground or by staining methods, and it is doubtful whether there are any constant morphological features by which the

Digitized by Google

organism may be distinguished from *L. morsus-muris* or *L. icteroides* Quite recently Noguchi has stated, as a result of cross-immunity experiments and serological tests, that the two organisms, *L. icteroides* and *icterohæmorrhagiæ*, are closely related, but not identical. The Pfeiffer reaction gives the sharpest differentiation between the two, but a monovalent *icteroides* immune serum will agglutinate slightly cultures of *icterohæmorrhagiæ*. The organism may be demonstrated without difficulty by the dark-ground illumination or by Burri's indian-ink method, and it readily stains with Löffler's methylene-blue and other aniline dyes. In microscopic sections of infected organs the leptospiras show up well with Levaditi's method of silver-nitrate impregnation. In order to indicate the peculiar minute elementary spirals running throughout the body, Noguchi has suggested that this organism should be regarded as the type of the genus he has named *Leptospira*; the presence of these spirals is a feature which distinguishes the organism from the other spirochætes.

The organisms exhibit rapid movements; when free, one end is extended and straight, the other semicircularly hooked, so that they progress in the direction of the straight portion and appear to be propelled from the rear by means of the rotating hook.

This parasite has been cultivated by Noguchi on solid media such as blood-agar or gelatin, but growth occurs most readily in fluid media which contain suitable animal or human serum; multiplication takes place rapidly in Ringer's solution containing one-third rabbit serum, the whole being covered with a thin layer of sterile liquid paraffin. The medium should be slightly alkaline and inoculated with a small quantity of the suspected blood. The optimum temperature is 30–37° C.; the organism can remain active for a long time at 10° C. It is an obligatory aerobe, unable to grow in the absence of oxygen. It is very sensitive to the destructive action of bile, bile-salts, and sodium oleate, but resists the action of saponin—in this last respect differing from many other spirochætes.

Its natural reservoir is the rat, in which it occurs in the fæces, urine, and kidneys, though it has not yet been microscopically demonstrated in the blood. It is believed that the disease was originally epizootic in rats, but that these animals have now become tolerant. In Japan it has been demonstrated in 32·4 per cent. of wild rats, and to a less degree in France, Tunis, Algiers, and in 4 per cent. of sewer rats in London (Foulerton). It is possible that some parasitic insect may play a part in the dissemination of the disease, though this has not been proved.

Digitized by Google

Probably the portal of entry is through skin abrasions. Courment and Durand have infected guinea-pigs by rubbing in cultures through the depilated skin.

Guinea-pigs are very susceptible to infection, and so also, but to a lesser degree, are puppies, rabbits, and monkeys. In order to reproduce the disease in these animals, 3–5 c.c. of the patient's blood are required.

Symptoms.—The incubation period in experimental animals is from five to six days. In man the onset is acute, with rigors, vomiting, headache, diarrhœa, and abdominal pains. A few hours later, fever with thirst and a general aching of the limbs ensue. The pyrexia is of an irregular type, between 103° and 105° F., falling by lysis about the tenth or eleventh day. Convalescence is established in the third week. Jaundice, when present, is noted in from 48 to 72 hours from the onset, and may be ushered in by hæmorrhages into the conjunctivæ or skin, or even from the mucous surfaces. The skin is lemon- or orange-coloured, rarely greenish in hue; pruritus is rare. Later, papular rashes may appear. Herpes labialis, which may be hæmorrhagic, is common.

The urine is highly coloured and nearly always contains albumen and bile, and sometimes casts and red blood-corpuscles as well. The leptospira may be demonstrated from the twelfth day onwards in blood-films, though in sparse numbers, but more readily in the centrifugalized urinary deposit. It is most numerous from the fifteenth to the twenty-third day. It may persist as long as 40 or even 100 days. Prostration may be extreme. Constipation is the rule; the fæces are pale in colour. The pulse is slow in the later stages and the blood-pressure low; a polymorphonuclear leucocytosis is present; later there is said to be an increase in the lymphocytes.

After three or four days, in mild cases, the fever subsides by lysis. Slight or even severe febrile relapses are often seen at the beginning of the third week.

The liver, and in rare cases the spleen, may be enlarged; the gall-bladder is distended, and tender on palpation; the lymphatic glands, more especially the inguinal and axillary, are frequently palpable.

Typhoidal, uræmic, and meningeal forms, all of great gravity, have been described. In the meningeal the cerebro-spinal fluid is under pressure and contains an excess of albumen, and the leptospira may be demonstrated in it in large numbers.

Epistaxis, hæmaturia, melæna, and hæmoptysis have been noted as complications, and also inflammatory ocular changes, such as

Digitized by Google

iritis and irido-cyclitis. A secondary fever may occur about the seventeenth day without the recurrence of jaundice. The sequelæ are anæmia and debility.

Diagnosis.—The urine from the fifth to the eighth day is said to give an intense green reaction when one or two drops of acetic acid are added. Early in the disease, if possible before the third day, the blood should be examined under the dark illumination for leptospira, and in doubtful cases the blood should be inoculated into guinea-pigs for confirmation. The diagnosis has to be established from yellow fever, catarrhal jaundice, syphilitic disease of the liver, the icterus of relapsing fever and of malaria. The fever must be distinguished from that of relapsing and yellow fevers, and the leptospira from *Spironema recurrentis*.

Diff Diag.

In various acute specific fevers, such as typhus, cerebro-spinal fever, and in several other fevers in which relapse may occur, including plague, rat-bite fever, and paratyphoid, especially paratyphoid-B, jaundice may occur as a complication. As a means of differentiating between infectious jaundice and the enteric group the atropine test of Marris (p. 304) may be employed. The complement-deviation test is the same as for syphilis—that is to say, in the acute stage of the disease the Wassermann reaction is positive.

An agglutination test for this disease has been devised by Martin, Pettit, and Vaudremer, using a culture of the leptospira grown on solid media; it occurs in a titre of 1 in 500, and even as high as 1 in 1,000. The specific agglutinins appear in the serum as early as the sixth, more generally about the tenth day of the illness, and persist for as long as twenty-two months.

The centrifugalized deposit of urine rich in these parasites may be utilized in place of a culture, and the diagnosis of infectious jaundice has by these means been placed upon a scientific if not a practical basis.

An antispirochætic serum specific for the *Leptospira icterohæmorrhagiæ* has now been prepared, and by this means the identification of the organism has been made possible.

Pathological anatomy.—The liver is invariably increased in size and may weigh 100-150 oz. The gall-bladder is generally half-filled with brown or greenish-brown bile; no blockage of the biliary ducts has been ascertained. The various microscopic lesions may be reduced to three main types. In the first there is little destruction of the parenchyma or intercellular tissue; the second is characterized by extreme cellular degeneration; in the third there is a localized destruction of glandular tissue. The fatty degeneration of the liver in Weil's disease is moderate in degree,

Digitized by Google

but cannot compare with that seen in acute yellow atrophy. The leptospiras can be demonstrated in large numbers among the secretory cells of this organ. The spleen may be enlarged and the glandular substance soft and diffluent. A generalized enlargement of the lymphatic glands, especially at the hilum of the liver, with hyperplasia and multiplication of the mononuclear cells, has been noted. Hæmorrhages occur in the kidneys, mostly in the intertubular tissues; later in the disease the microscopic picture may resemble that of early interstitial nephritis, and the leptospira may be demonstrated in great profusion. The bone-marrow exhibits considerable changes, proliferation of the myelocytes, deposition of pigment in the microphage cells, and diminished activity of the hæmatopoietic system being the chief points. There are submucous petechiæ in stomach and duodenum, and hæmorrhagic patches in the lungs.

Treatment is at present mostly symptomatic. Salvarsan and its modifications have apparently little or no effect. An attempt should be made to eliminate the toxins by flushing out the bowel by means of small repeated doses of calomel and by intravenous injections of normal saline containing 5–10 per cent. of glucose. The serum of patients convalescent from this disease has been injected in daily doses of 30–40 c.c. by the intramuscular route as a means of combating the disease. Hexamine (urotropin) in 10-gr. doses given repeatedly has been exhibited on purely empirical grounds, in some cases with a satisfactory result.

A polyvalent anti-icterohæmorrhagiæ horse-serum has now been prepared by Inada and Ido, which possesses marked protective properties and will probably be employed in the treatment of Weil's disease.

Prophylaxis manifestly consists in sterilizing the fæcal and urinary discharges of the patients, and in waging war against the rat, the natural host of the parasite, and carefully guarding against its access to food. Noguchi has prepared a vaccine of killed cultures of leptospira with which he has been able to produce a certain degree of immunity in guinea-pigs.

Digitized by Google

CHAPTER XII

RAT-BITE FEVER

Synonyms.—Sodoku ; Sokiosa (Japanese).

Definition.—An acute febrile disease caused by a spirochæte, *Leptospira morsus-muris*, inoculated into man by the bite of an infected rat, causing a local disturbance at the site of infection, followed by a general fever, with a tendency to relapse and, in some cases, a cutaneous eruption.

History.—This comparatively rare disease has long been known to Japanese physicians. Since its recognition cases have been reported from other countries.

In 1915 Futaki, Takaki, Taniguchi, and Osumi demonstrated long slender spirochætes in the lymphatic glands from the tenth to the thirteenth day of the illness ; later they found similar, though shorter and stouter, organisms in the bloodstream ; these latter are now recognized as being the young forms of the parasite. This work has since been confirmed by Kaneko and Okuda in 1917.

Geographical distribution.—Rat-bite fever appears to have a widespread distribution, but it is especially common in Japan. Cases have been reported from Great Britain by Horder and Atkinson, from the United States, from Germany, from Italy, from Australia, and one by Low from East Africa.

Etiology.—*L. morsus-muris* is a long slender spirochæte morphologically similar to the *L. icteroides* of yellow fever, *L. icterohæmorrhagiæ* of infectious jaundice, and *L. hebdomadalis* of seven-day fever. The leptospira is 2–5 μ in length ; on cultivation on appropriate media (p. 194) the organism becomes longer, up to 19 μ. The curves are regular and generally number three or four. The leptospira is most easily demonstrated in the blood by means of the ultramicroscope. Similarly it may be seen in the exudate in the neighbourhood of the bite, and in the juice from the superficial lymphatic glands. Its presence can be easily verified in suspicious cases by inoculation of white mice from any of this material. Next to mice, white rats and guinea-pigs are most susceptible. Usually the experimental animals survive. The organisms appear in the bloodstream about seven days after inoculation, and persist for several months. The disease can be transmitted by the brown rat (*Rattus norvegicus*), the black rat

Digitized by Google

(*R. rattus* and *R. alexandrinus*), and by the bite of a ferret or of a cat. About 3 per cent. of the house-rats in Japan are natural carriers of the parasite.

Symptoms.—The incubation period varies from one to sixty days; the average being 5–10 days, during which time the wound heals. The cicatrix itself, and sometimes the surrounding tissues, become inflamed, with formation of blebs and even necrosis. The lymphatics draining the area are implicated and the glands themselves become swollen and tender. The onset of the fever is characterized by rigors and malaise; the temperature gradually rises in three days to a maximum of 103–4° F., and after a further period of three days ends in crisis with profuse sweating.

After the primary attack a quiescent interval of five to ten days ensues, with subsidence of the local disturbance. One or more relapses, associated with the same symptoms, and in addition a characteristic purple papular exanthem or urticaria on the chest and arms, have been noted.

In most cases the reflexes are increased; there may be pains in the muscles and joints, and hyperæsthesias and œdema of various parts of the body. The death-rate is about 10 per cent. The end is ushered in by delirium, often lapsing into coma.

As in the case of relapsing fever, the organism can be demonstrated in the blood only during the fever, and disappears during the apyretic intervals. The serum agglutinates the leptospira in low dilutions. There is an eosinophilia during the paroxysm and a moderate leucocytosis of about 15,000. It is said that the serum of this disease gives a weak positive Wassermann reaction.

Pathology.—In the fatal cases the lymph-glands are swollen, the spleen is enlarged, the liver hyperæmic, and the lungs may show hæmorrhages. The cornea is often involved. The spirochætes have been demonstrated in the liver, spleen, kidneys, suprarenal glands, eyes, and testicles.

Differential diagnosis.—This has manifestly to be made from the different forms of relapsing fever and trench fever, with which the temperature chart has much in common. In tropical countries the possibility of a coexistent malarial infection has to be taken into account. The puffiness of the face accompanying the urticarial eruption may simulate Bright's disease.

Treatment.—Hata has reported beneficial results from the intravenous injection of salvarsan, and Low has recently reported a cure with graduated doses (0·4 to 0·9 grm.) of novarsenobillon. Otherwise the treatment is a purely symptomatic one. As a prophylactic measure a rat bite should be cauterized.

Digitized by Google

CHAPTER XIII

SEVEN-DAY FEVER

Synonyms.—Nanukayami ; Shueki ; Saku Fever (Japanese).

Definition.—A short fever occurring epidemically during the summer months, especially in Indian ports and in Japan (Fukuoka), and characterized by sudden invasion, severe headache, pains in the back and limbs, and pyrexia of a peculiar saddle-back type—occasionally of a continued type—lasting from six to seven days and associated with a pulse which is relatively slow in relation to temperature. The etiological cause of the disease appears to be the recently discovered *Leptospira hebdomadalis.*

History.—Possibly this fever is one of several fevers included under the somewhat comprehensive term " simple continued fever." Rogers, by a careful study of a vast number of cases of fever in Calcutta, observing that this particular type has a definite seasonal incidence—the late hot weather and the early monsoon months in Calcutta—and declines just at the time when the principal malarial rise of the year takes place, concluded from this and from the absence of malarial parasites that it cannot be malarial, from the absence of respiratory symptoms that it is not influenza, and from the absence of violent joint-pains and eruption that it cannot be dengue. In 1918 Ido, Ito, and Wani described a spirochæte (*L. hebdomadalis*) as the specific cause of the fever.

Geographical distribution.—It is now known that the disease is not confined to India. Cases conforming to Rogers's original description have been recorded from Panama, Mediterranean ports, Ceylon, Japan, and by Archibald from the Sudan.

Symptoms.—The symptoms resemble those of infectious jaundice, and the blood shows a definite leucopenia. According to Rogers a mottled rash appears in about 7 per cent. of cases from the fourth to the sixth day of the disease. It is confined to the extensor aspect of the forearm and is not followed by desquamation. This exanthem is apt to be mistaken for measles or for dengue. The disease usually begins amongst the sailors and spreads later to the townspeople. It occurs in Indian ports, but is probably unknown in the interior of the country. Apparently it is a mild disease, has no mortality, and no distinctive pathological anatomy.

Digitized by Google

The organisms can be demonstrated in considerable numbers in the urine of patients after the eighth day and they may persist to the thirty-ninth day.

Etiology.—*L. hebdomadalis* resembles *L. icterohæmorrhagiæ* very closely, but can be distinguished from it by serological reactions. It is present, though in small numbers, in the bloodstream during the pyrexial period, and may be demonstrated by means of Leishman's stain or by the dark-ground illumination. The chief channel of elimination is by way of the kidneys and urine. The organism may be readily cultivated by Noguchi's method.

The blood of convalescents from seven-day fever contains specific immune and spirochæticidal bodies, and when injected, together with a culture of the organism, into the peritoneal cavity of a guinea-pig a positive Pfeiffer reaction is obtained. Young guinea-pigs are susceptible to inoculation with the blood of patients and with cultures of the spirochætes; they may also be infected via the skin or *per os*.

The field-mouse (*Microtus montebelli*) would appear to be the normal host of this leptospira in Japan, and this organism can be detected in the kidneys and urine of 3·3 per cent. of these animals. The endemic area of prevalence of seven-day fever corresponds with the distribution of this mouse in Japan.

Some writers have confused this disease with dengue, with which they consider it to be identical, but, in view of the recent work of Cleland and Bradley on that disease, one can see no grounds for adopting this view. The bone-pains and the morbilliform rash in dengue are sufficient to distinguish it from seven-day fever.

Digitized by Google

CHAPTER XIV

DENGUE

Synonyms.—Dandy Fever (probably derived from the Spanish for "dandy"); Breakbone Fever; Scarlatina Rheumatica; Polka Fever (Brazil).

Definition.—A specific fever conveyed by *Stegomyia fasciata* and possibly other mosquitoes, occurring usually as a rapidly spreading epidemic; in typical cases, characterized by a suddenly developed primary fever of about three days' duration, succeeded by a period of apyrexia—actual or relative—and this again by a milder secondary fever accompanied by a rubeoloid eruption. Throughout the febrile stages, and often subsequently, severe rheumatic-like pains are a prominent symptom. The disease in its active form lasts about a week and is attended with little, if any, mortality.

Geographical distribution and mode of spread.—Most parts of the tropical world have been visited at one time or another by dengue. From a study of the dates of the various epidemics it would seem that there is a tendency for it to assume pandemic characters about once in every twenty years. Perhaps of all places in the world it is most frequently met with in the West Indies.

Dengue has appeared in Syria, Asia Minor, on the Ægean shòres of Greece and Turkey, and in North Queensland, Australia. Early in the last century it was seen in America, as far north as Charleston and Philadelphia in the United States, and as far south as São Paulo in the Brazils.

Like other specific communicable diseases, dengue tends to advance along trade routes and lines of communication. Thus, starting from Zanzibar, the epidemic of 1870–3 first reached Aden. Thence it travelled to Suez on the one side and to India on the other. Passing to Singapore, it followed the trade routes to Cochin China and China, spreading at the same time to the islands of the Eastern Archipelago. From India it was carried by the coolie ships to Mauritius and Réunion in 1873.

An epidemic which Manson witnessed in Amoy (1872) illustrated very well a characteristic feature of dengue epidemics—namely, the peculiar suddenness of their rise and extension, and the general

Digitized by Google

prevalence of the disease in an affected community ; in this particular epidemic quite 75 per cent. of natives and foreigners were attacked within a very few weeks. All ages and occupations, both sexes, and people in every condition of life, were alike subject to it. About the first week in August it was rumoured that a peculiar disease had appeared in the town ; by the end of the second week the cases were numerous, whole families being prostrated at a time. A week later the cases were still more numerous, and by the end of the month so general was the disease that the business of the town was seriously interfered with. By the end of the following month—that is to say, in about eight weeks from the first appearance of the epidemic—all the susceptible apparently had passed through it, and, so far as Amoy residents were concerned, the disease was at an end, cases occurring for a few weeks longer only in visitors from unaffected districts. This course seems to be fairly typical of all dengue epidemics. There should be no difficulty, then, in distinguishing an outbreak of this character from seven-day fever, a disease which Rogers and other Indian workers consider to be identical with it.

A big epidemic was studied in Formosa in 1915 ; a similar one was noted in the following year in Brazil and spread to Australia, especially Queensland. The disease may attack a large proportion of the population, as, for instance, 20,000 people in Galveston in 1897.

Etiology.—Various organisms, including an intracorpuscular parasite allied to *Babesia*, have been described, all on insufficient evidence. Graham, in Beirut, Syria, first suggested that the disease was transmitted by the agency of a mosquito, *Culex fatigans*. By taking mosquitoes which had fed on dengue blood to mountain villages where no mosquitoes existed, he was able to transmit the disease to volunteers. Acting on this hypothesis, he was able to protect families from dengue by means of mosquito-nets. Ross is said to have extinguished the yearly epidemics in Port Said by anti-mosquito measures. Experiments by Ashburn and Craig, made under favourable conditions, seemed to show that the germ of dengue resides in the liquor sanguinis, that it is ultramicroscopic and therefore filterable through a Chamberland filter, that injected into non-immunes it gives rise to typical dengue, that under natural conditions it is transmitted by *Culex fatigans* through the salivary glands, that the incubation period of the experimental disease is from three to fourteen days, and that it is not contagious in the ordinary sense of that word. In these and in some other respects dengue has a striking parallelism to yellow fever, a fact

Digitized by Google

which suggests the advisability of making extended researches for a possible causative spirochæte on the lines of Noguchi, though Cleland and his co-workers have as yet failed to find any leptospira or other organism with the dark-ground illumination method.

By a series of well-conceived and carefully-carried-out experiments, Cleland, Bradley, and MacDonald in Australia have now definitely proved that the virus of dengue is conveyed by *Stegomyia fasciata*, and have rendered it highly improbable that *Culex fatigans* is a vector. They have shown that the incubation period of the disease, dating from the infecting bite, is from six to eight, but may be as long as eighteen days. Furthermore, by subinoculation from one individual to another they transmitted the disease for four generations, and showed that the virus is present in the blood from the second to the fourteenth day of the disease. The virus does not appear to reside in any one element of the blood. Although, in view of recent work, *Stegomyia* must be regarded as much the most active transmitter of the disease, possibly *Culex fatigans* is a vicarious host.

It has to be noted that in 1917 Koizumi, Yamaguchi, and Tonomura, in the Formosan outbreak, incriminated other mosquitoes, such as *Stegomyia scutellaris* and *Desvoidea obturbans*, as intermediary hosts. These writers also showed that a very small amount—0·00005 c.c.—of dengue serum is capable of reproducing the disease and is lethal to guinea-pigs in 7–36 days, but that dengue cannot be transmitted to these animals for more than two generations.

Important points still undetermined are the duration of the infective stage in the blood, and the ripening process of the undetermined germ in the mosquito.

Influences of meteorological conditions.—When dengue spreads beyond its ordinary tropical limits, as, for example, in the epidemics of Philadelphia and Asia Minor, the extension occurs only during the hottest part of the year—in the late summer and early autumn. Hitherto such epidemics have been arrested on the approach of winter. Even when occurring within the tropics, dengue prevails principally, though not exclusively, during the hottest part of the year. High atmospheric temperature, therefore, seems to be one of the conditions it demands.

Epidemics occur generally after the rainy season, and in the Pacific islands, at any rate, the disease appears to have a seasonal incidence during the months of June, July, and August.

Usually a coast disease.—It would appear that dengue, like yellow fever, prefers the coast line and the deltas and valleys of

Digitized by Google

great rivers to the interior of continents. There are many exceptions to this rule; in 1870-3 it spread all over India. The distribution and concentration of population on the seaboard and along rivers, the freedom of communication between communities that are so located, and the mosquito conditions probably determine this preference.

As a rule, elevated places enjoy a relative immunity; if the disease is introduced into such localities it does not spread. To this, again, there are exceptions, for the Syrian epidemic referred to prevailed in certain spots 4,000 to 5,000 ft. above the sea. In the Mediterranean basin dengue is a disease of autumn months and generally follows the summer outbreak of phlebotomus fever.

Symptoms.—The *incubation period* seems to be somewhat variable, generally 5-9 days, though sometimes it appears to be less. The course of the disease may be divided into three periods—(*a*) the stage of invasion, lasting 2-3 days; (*b*) the stage of remission, lasting 12 hours to 3 days; (*c*) the terminal fever and eruption.

Stage of invasion.—An attack of dengue may be preceded for a few hours by a feeling of malaise or, perhaps, by painful rheumatic-like twinges in a limb, toe, finger, or joint. Usually it sets in quite suddenly. One patient, describing his experience, said that in the morning he got up feeling quite well, but before he could complete his dressing he was so prostrated by pain and fever that further exertion was impossible and he had to crawl back to bed again. Similar stories, illustrative of the sudden incidence of the symptoms, circulate during every epidemic of dengue. Sometimes the fever is ushered in by a feeling of chilliness or even by a smart rigor; sometimes a deep flushing of the face is the first sign of the disease.

However introduced, fever rapidly increases. The head and eyeballs ache excessively, and some limb or joint, or even the whole body, is racked with peculiar stiff, rheumatic-like pains, which, as the patient soon discovers, are very much aggravated by movement. The loins are the seat of great discomfort, amounting in some cases to actual pain; the face—particularly the lower part of the forehead, round the eyes, and over the malar bones—may become suffused a deep purple; and often the skin over part or the whole of the body, and all visible mucous surfaces, are more or less flushed, that of the mouth and throat being sore from congestion and perhaps from small superficial erosions. The eyes are usually much injected; very often the whole face is bloated and swollen. This congested, hypersensitive, and erythematous state of the skin constitutes the so-called prodromal eruption. There may be a *tache cérébrale*.

Digitized by Google

These symptoms becoming in severe cases rapidly intensified, the patient, in a few hours, is completely prostrated. His pulse has risen to 120 or over; his temperature to 103° F., in some cases to 105°, or even to 106°. He is unable to move owing to the intense headache, the severe pain in limbs and loins, and the profound sense of febrile prostration. From time to time the skin may be moistened by an abortive perspiration, but for the most part it is hot and dry. Gastric oppression is apt to be urgent, and vomiting may occur. Gradually the tongue acquires a moist, creamy fur which, as the fever progresses, tends to become dry and yellow. (Chart 10.)

In this condition the patient may continue from one to three or four days, the fever declining somewhat after the first day. In the vast majority of cases this, the first and most acute stage, is abruptly terminated about the end of the second day by crisis of diaphoresis, diarrhœa, diuresis, or epistaxis. When epistaxis occurs the relief to the headache is great and immediate. On the occurrence of crisis the erythematous condition of the skin, if it has not already disappeared, rapidly subsides. In a proportion of cases, and particularly in certain epidemics, crisis does not occur, the fever slowly declining during a period of three or four days. Thus the urgent symptoms abate, and the patient rapidly, or more slowly, passes from what in many cases may be described as the agony of the first stage to the comparative calm and comfort of the second.

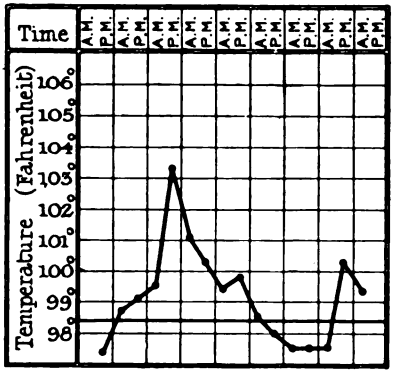


Chart 10.—Dengue. (*After Cleland and Bradley.*)

Stage of remission.—When the second stage is established and the thermometer has sunk to normal, the patient is sufficiently well to leave his bed and even to attend to business. An occasional twinge in leg, arm, or finger, or a tenderness of the soles of the feet, and perhaps giddiness in walking, may remind him of what he has gone through and warn him that he is not quite well yet. But the tongue clears, and the appetite and sense of well-being return to some extent.

Terminal fever and eruption.—This state of comparatively good health continues to the fourth, fifth, sixth, or even to the seventh day, counting from the commencement of the illness. Then there

Digitized by Google

is generally a return of fever, slight in most cases, more severe in others. It is usually of very short duration—a few hours. Sometimes this secondary fever does not occur; probably it is often overlooked. With the recurrence of the fever an eruption of a rubeolar character, consisting of dark, dusky spots, appears. The pains likewise return, perhaps in more than their original severity. Though the fever subsides in a few hours, the eruption, at times very evanescent, may keep out for two or three days longer, to be followed very generally by an imperfect furfuraceous desquamation. It seldom happens that the fever or pains at this stage keep the patient in bed, although that is the best place for him if a comfortable and speedy convalescence is desired. Rarely, in this secondary fever, does the thermometer rise to 103° F. The temperature falls rapidly to below normal on the setting-in of diaphoresis, or of diarrhœa, or of some form of crisis.

Characters of the eruption.—The terminal eruption of dengue possesses very definite characters. It is absent in a very few cases only; in many of those cases in which it is supposed to be absent, being slight, it is overlooked. As stated, the eruption is rubeolar in character. It usually commences on the palms and backs of the hands, extending for a short distance up the forearms. Its development is often associated with sensations of pricking and tingling. On the palms of the hands the spots are at first about the size of a small pea, circular, dusky red, and sometimes slightly elevated. The eruption quickly extends, and is best seen on the back, chest, upper arms, and thighs. In these situations it appears at first as isolated, slightly elevated, circular, reddish-brown, rubeoloid spots, from one-eighth to one-half of an inch in diameter, thickly scattered over the surface, each spot being isolated and surrounded by sound skin. After a time the spots, enlarging, may coalesce in places; thus irregular red patches from 1 to 3 in. in diameter are formed. Or perhaps there is a general coalescence of spots, isolating here and there patches of sound skin; in this case the islands of sound skin give rise, at first sight, to the impression that they constitute the eruption—a pale eruption, as it were, on a scarlet ground. In a few instances the whole integument may be covered with one unbroken sheet of red. The rash is usually most profuse on the hands, wrists, elbows, and knees; in these situations it is generally coalescent, and there, too, it may be detected though absent elsewhere. The spots disappear on pressure, and never or rarely become petechial. They fade in the order in which they appear—first on the wrist and hands; then on the neck, face, thighs, and body; last on the legs and feet.

Digitized by Google

DENGUE RASH.

(Partly after Cleland and Bradley, by permission.)

Digitized by Google

Digitized by Google

Slowing of the pulse as the fever advances, and leucopenia as in yellow fever, have been remarked. The main characteristic of the dengue rash has been described as "midway between scarlet fever and measles, but less definite." (Plate XIV.)

Desquamation.—Desquamation may go on for two or three weeks. In many it is trifling in amount; for the most part it is furfuraceous. Rarely does the epidermis peel off in flakes of any magnitude; never in the broad sheets seen after scarlatina. Often for a day or two desquamation is accompanied by intense pruritus.

Convalescence.—In some instances, and in some epidemics, the disease terminates with the fading of the eruption; appetite and strength gradually return, and the patient, after a few days of debility, feels well again. Bradycardia and mental depression may persist for a time.

The rheumatoid pains.—With most, their troubles do not end so soon. For days or weeks some muscle, tendon, or joint is the seat of peculiar pains, which may become so severe as to send their victim back to bed again. Sometimes, three or four weeks after all apparent trace of the disease has vanished, a joint or a muscle will be suddenly disabled by an attack of this description. This may occur in patients who, during the acute stage, suffered little or no pain. A finger or toe, or a joint of a finger or of a toe, may alone suffer. Of all the joints, perhaps the knee is most frequently affected; but wrists or shoulders are often attacked, and their associated muscles may even undergo considerable atrophy from enforced disuse. The soles of the feet, too, and the tarsal articulations are favourite sites.

The pains of dengue—those occurring during the initial fever as well as those that may be regarded as sequelæ—are difficult to locate with precision; the joints or muscles affected may be percussed, pressed, or moved with impunity.

The pains are usually worst on getting out of bed in the morning, and on moving the affected part after it has been at rest for some time; they are relieved somewhat by rest and warmth. Passive movements are, as stated, not painful, but any resistance to the movement of the limb may cause acute suffering. When a muscle is affected the pain is accompanied by a sense of powerlessness. The pains have been well described as "the earliest harbinger, the persistent companion, and the last vestige of the disease."

Other complications and sequelæ.—Convalescence may be very much delayed by the persistence of these pains; also by anorexia, by general debility, mental depression, sleeplessness, evanescent feverish attacks, boils, urticarial, lichenoid, and papular eruptions,

Digitized by Google

and by troublesome pruritus. Among sequelæ and complications may be mentioned enlargement of the lymphatic glands (particularly the superficial cervical), orchitis, possibly endocarditis and pericarditis, hyperpyrexia, purpura, and hæmorrhages from the mouth, nose, bowel, and uterus. Miscarriage is rare. The urine sometimes contains a trace of albumen, but true nephritis does not occur.

Variability of epidemic type.—Judging from the published descriptions, there is considerable variety in the symptoms of this disease in different places and in different epidemics. Some authors mention swelling and redness of one or more joints as a common and prominent symptom; others refer to metastasis of the pains, enlargement of submaxillary glands, orchitis, mental depression, hæmorrhages, and so forth, as being frequently present. However this may be, the essential symptoms in well-marked cases are the same practically everywhere, and in all epidemics; these are, suddenness of the rise of temperature, an initial stage of skin congestion, limb and joint pains, and a terminal rubeoloid eruption.

Relapses are not uncommon in dengue, and second and even third attacks during the same epidemic have been recorded. As a rule, however, susceptibility to the disease is exhausted by one attack. According to Hare, in a recent Australian epidemic the immunity acquired by an attack did not persist beyond one year.

Mortality.—In uncomplicated dengue the mortality may be said to be almost nil (0·1 per cent., Hare). In the case of very young children, convulsions and delirium may occur and cause anxiety; and in the aged and infirm, and in those suffering from chronic exhausting disease, an attack of dengue may prove a serious complication. Some writers state that the gravity of any given case is in direct proportion to the abundance of the eruption; others deny this.

In Europeans an attack of dengue very often leads to a condition of debility necessitating temporary change of climate, or even return to Europe. In both Europeans and natives the attendant lowering of the resisting powers predisposes to other and more dangerous diseases.

Morbid anatomy.—On account of the low mortality, post-mortem records are few. In the autopsies recorded, localized pulmonary and intracranial inflammation were the special features. Serous effusions in the neighbourhood of joints and inflammation of the crucial ligament of the knee have also been noted.

Diagnosis.—Dengue must not be confounded with yellow fever, rötheln, scarlatina, measles, syphilitic roseola, influenza,

Digitized by Google

cerebro-spinal meningitis, typhus, hæmorrhagic smallpox, enteric, phlebotomus fever, seven-day fever, rheumatic or malarial fever. A knowledge of the distinctive features of these diseases, and the fact that dengue is attended with a rash and with articular pains, and that it occurs in great and rapidly spreading epidemics, should prevent any serious error in diagnosis. According to Ashburn and Craig, there is a well-marked leucopenia in dengue averaging 3,800 per c.mm., with relative increase of the small lymphocytes. This in some circumstances may prove an aid to diagnosis. Typhus often presents a difficulty; the more serious condition of the patient, the high remittent temperature, the petechial character and distribution of the rash, and the Weil-Felix reaction in the latter disease will help in differentiation.

Treatment.—Were it possible to secure perfect isolation and inmunity from mosquito bite for the individual during an epidemic of dengue, doubtless he would escape the disease. Even comparative isolation is attended with diminished liability.

Like the allied fevers, dengue runs a definite course; therefore it is useless to attempt to cut it short. The patient should go to bed as soon as he feels ill, and should keep his room till the terminal eruption has quite disappeared and he feels well again. Ten days is not too long to allow in severe attacks. As in influenza, light liquid diet, rest, and the avoidance of chill conduce powerfully to a speedy and sound convalescence. At the outset of the fever some saline diaphoretic mixture, with aconite, may be prescribed with advantage. If the pains be severe and the fever high, antipyrin, or phenacetin, or belladonna will give great relief. Cold applications to the head are comforting. If the temperature rises to 105° F. or over, cold sponging or the cold bath ought to be had recourse to. If the pains continue very distressing, a hypodermic injection of a minute dose ($\frac{1}{10}$ gr.) of morphia will afford welcome relief and do no harm. Purgatives and emetics should be avoided unless pronounced constipation, or a history of surfeit, urgently demands their exhibition. The pain caused by the muscular movements entailed by the efficient action of purgatives more than counterbalances any advantage the latter might otherwise bring. Wine in the early stage is not advisable. Freshly made lemonade, or iced water, will be found an acceptable drink during the fever.

For the pains experienced during convalescence, rubbing with opium or belladonna liniment, gentle massage, electricity, salicylates, small doses of iodide of potassium and quinine, have been advocated. Debility, or anorexia, indicates tonics such as quinine, strychnine, mineral acids, or vegetable bitters, and change of air.

Digitized by Google

CHAPTER XV

PHLEBOTOMUS FEVER

Synonyms.—Papataci Fever; Three-day Fever; Sandfly Fever; "Dog Disease."

Definition.—A specific fever of short duration and no mortality caused by a germ—possibly ultramicroscopic—introduced by the bite of the sandfly (*Phlebotomus*).

History.—This disease has been recognized clinically for upwards of a century and described under a variety of local names; but its definite relation to its transmitting agent, although suspected by McCarrison in Chitral in 1903, was not established till 1908, when Doerr published his observations of the infectivity of the blood in this form of fever and the rôle of the sandfly as transmitter. Doerr's conclusions have been definitely confirmed by Kilroy, who exposed himself for five nights to the bites of sandflies on Suda Island, where these insects are particularly abundant and where phlebotomus fever is prevalent; subsequently, at the end of the first day of his fever, he injected his blood into a healthy man and thereby communicated the disease to him.

Geographical and seasonal distribution.—The range of phlebotomus fever is probably coextensive with that of the insect transmitter. In the tropics it may break out at any time as an epidemic amongst new arrivals; in the subtropics it occurs only or principally during the summer and early autumn. Where the phlebotomus is absent, e.g. Bermuda, this fever is not found. In some phlebotomus-haunted places as many as 50 per cent. of newcomers are attacked. The disease was much in evidence during the recent War, in Gallipoli, Salonika, the Ægean Islands, Egypt, Palestine, Syria, Mesopotamia, and India, but there is no record of its occurrence among troops in East Africa.

Etiology.—The germ resides in the blood of the patient during the first day of the fever. It is ultramicroscopic, passing through filters which arrest *Micrococcus melitensis*. According to Doerr it is transmitted hereditarily through the egg and larva of phlebotomus to the imago; this, however, has not been firmly established experimentally. A short sharp fever has been produced in monkeys after intravenous injection of sandfly-fever blood.

Digitized by Google

Representatives of the genus *Phlebotomus* are to be found in most tropical and subtropical countries. The various species are usually designated "sandflies." They are exceedingly minute, very delicate, yellowish, greyish, or brownish, somewhat slenderly built insects that bite principally during the night and that can pass easily through the meshes of an ordinary mosquito-net. They dislike sunlight, but at night-time are readily attracted by lamps or candles. At rest the wings are uplifted (Fig. 66). The legs are long and slender; the wings, body, and antennæ are thickly covered with short hairs. The joints of the antennæ are con-

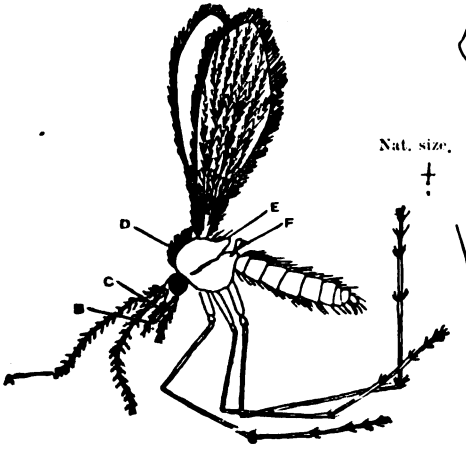


Fig. 66.—Female phlebotomus. (*After Alcock.*)

A, Antenna; B, palps; C, proboscis; D, prothorax; E, mesothorax; F, halteres

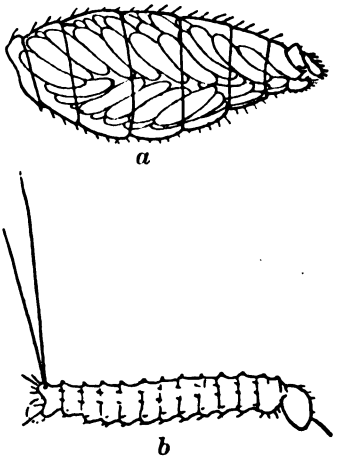


Fig. 67.—*a*, Abdomen of female phlebotomus, showing eggs; *b*, young phlebotomus. (*After Alcock.*)

stricted. The proboscis is as long as the head. The tips of the piercing apparatus (which in other respects resembles that of the mosquito) project beyond the labium. The leaf-shaped wings are somewhat narrow, and show all three branches of the second longitudinal vein very distinctly. The powers of flight are feeble; more usually the insects progress by a series of short skips. Their bites are painful and lumps or even vesicles may form, and the irritation may interfere with sleep.

P. papatasii (the species on which Doerr's observations were made—hence one of the names for the disease, papataci fever) lays about forty eggs, selecting for the purpose damp localities such as the walls of cellars, of latrines, cesspools, crevices in walls, caves,

Digitized by Google

and embankments. The cycle of egg, larva, and imago takes about one month in warm and upwards of two months in cooler weather to complete. (Fig. 67.) Probably the duration of the life of the imago is not a long one, though Wenyon succeeded in keeping a solitary specimen alive for fifty-six days; their usual span of life in captivity is under fifteen days.

There has been much confusion in the nomenclature of the various species of *Phlebotomus*, and it has not been determined which of them, other than *P. papatasii*, convey the infection. The insect becomes capable of transmitting the infection after an incubation period of six days within its body. It has been suggested that the horse acts as a reservoir of virus.

Pathology.—Yellow fever, dengue, and phlebotomus fever have several important points in common; a circumstance suggestive of the possibility of a common or, at all events, a similar origin —for instance, a leptospira as in the first-named. Each is transmitted by an insect; their germs occur in the bloodstream and are filterable; they are diseases of warm climates only; and, clinically, they are characterized by a short incubation period, a short and rapidly developed fever which is usually associated with relatively slow pulse and leucopenia, and relative decrease of the polynuclears. It would be interesting to ascertain if these diseases are mutually protective.

Symptoms.—After an incubation period of from four to seven days, with or without a prodromal stage, the fever is ushered in by slight or more severe rigor. The face becomes flushed and swollen, frontal headache is intense, and there is usually severe general aching. Pain at the back of the eyes, accentuated by pressure on the globes or by the least movement of the head, is characteristic. There are influenzal pains in the back and legs and general stiffness of the muscles. The patient is drowsy, but suffers from insomnia. The conjunctivæ are so injected that they have been likened to those of a mastiff. The tongue has a central fur. The fauces and palate are often congested, and are studded with small vesicles. In from twenty-four to thirty-six hours the temperature has reached 103–4° F. It keeps about this point for a day longer, and then begins to fall, with or without epistaxis, vomiting, sweating, or diarrhœa, reaching the normal about the end of the third or beginning of the fourth day. The patient continues debilitated, especially mentally, for a week or two longer.

The blood picture shows a slight leucopenia without serious alteration in the number of mononuclears. The pulse-rate is relatively slow.

Digitized by Google

Serious complications do not occur, but in some years diarrhœa, in other years pharyngitis, are features of the epidemic. An attack would seem to confer a certain amount of immunity, though second attacks are by no means uncommon.

There are no important sequelæ. Desquamation is very rare; a point which, together with the absence of an eruption, serves to differentiate this fever from dengue, a disease resembling it in many respects. The mortality is nil in the healthy.

Diagnosis.—It is extremely difficult in the early stages to distinguish this fever on clinical grounds from malaria—especially subtertian, from paratyphoid, dengue, typhus, and influenza. In typhus the greater hebetude and in influenza the respiratory catarrh must be taken into consideration.

Treatment.—The most valuable drug in the treatment of sandfly fever is opium; 30 drops of the liquor opii sedativus may be given at the onset. It greatly relieves the headache.

As it would appear that three-day fever is a disease of locality, houses and places believed to be infected should be avoided, and, where possible, disinfected.

With a view to diminishing the local sandfly pest, all rubbish should be burned or otherwise got rid of, ruinous walls should be demolished, latrines smoked with sulphur fumes and put into sanitary condition, dark damp places dried, whitewashed, and ventilated. By these and similar measures much can be done to control the infection. Unfortunately, a mosquito-net having a mesh sufficiently small (i.e. 22 holes to the linear inch) to keep out sandflies is intolerable to a white man in a hot climate. As the phlebotomus does not fly higher than 10 ft., the removal of inmates to an upper storey is a very effectual preventive measure. It is said that a lump of camphor placed in the bed repels the insects, as they dislike the odour. Of the repellent ointments in use for application to the skin the following is considered the most efficacious (Balfour):—

℞ Ol. anisi Ol. eucalypti Ol. terebinth.	āā ℥iii.
Lanolini	℥i.

Characters of the Genus Phlebotomus

Small hairy flies from 1·5 to 2·5 mm. in length, easily recognized by their form and thick hairy coat. Only the females suck blood; in some people the bite causes a considerable local disturbance, in others little or none.

The greater part of the body is covered with long yellow hairs, for the most part, probably, modified scales. The antennæ have sixteen joints. The

Digitized by Google

proboscis is as long as the head and contains a number of piercing organs.

The wings are definitely pointed, and on removal of the outer coating of scales the venation can be seen. The insect possesses six slender legs. The abdomen is divided into ten segments.

In the *female* the abdomen is spindle-shaped, and is provided with an upper and a lower pair of small claspers. In the *male* there are five pairs of sexual appendages—the upper and lower claspers, and various other structures known as the "submedian lamellæ," "intermediate appendages," and "intromittent organ" (Newstead).

The female lays her eggs in rubble walls and in caves. The eggs, six to nine days after being laid, hatch into twelve-segmented caterpillar-like larvæ (Fig. 67, *b*), further characterized by two pairs of bristles on the posterior extremity and by the absence of eyes or organs of locomotion. According to Howlett, the eggs of different species of *Phlebotomus* can be differentiated by the reticular pattern on the shell; the newly hatched larvæ may also be differentiated by their outlines and size of bristles. In six to eight weeks the larvæ are 0·5 mm. in length, and feed on organic detritus and algæ. The pupæ are fixed in crevices of stones, slates, etc., the imagines emerging after fourteen days (Marett).

In the classification of these insects, entomologists have relied on the slender differences afforded by the venation of the wings, the length of segments of the palps, the number and arrangement of the bristles or spines on the claspers. Up to the present there has been little agreement on this subject.

Great care must be exercised in the preservation of specimens for identification. The insects should be placed in a web-like layer of teased cotton-wool, but must not be *covered* with the wool, as even such slight pressure breaks their appendages.

Digitized by Google

CHAPTER XVI

SPOTTED FEVER OF THE ROCKY MOUNTAINS

Synonyms.—Rocky Mountain Fever; Black Fever; Blue Disease.

Definition.—A specific fever resembling symptomatically typhus exanthematicus, supervening on the bite of a tick—*Dermacentor venustus*, Banks.

History.—For upwards of thirty years a peculiar disease variously named "spotted fever," "blue disease," "black fever," has been recognized as endemic in limited districts of Montana and Idaho, United States of America. It was first described by Wood, in 1896, and later by Maxey, in 1899, as a distinct disease, and in the spring of 1902 it was investigated by Wilson and Chowning, who attributed it to the presence in the blood of a parasite akin to the piroplasma of Texas cattle fever. Their results were endorsed by Wesbrook, Cobb and Anderson; but in May, 1904, Wardell Stiles failed to recognize the parasite, either in fresh preparations of the blood or in the preparations of previous investigators. Other observers have been equally unsuccessful; the existence of the so-called *Pyrosoma hominis* is now discredited, and the question of the germ-cause of Rocky Mountain fever has been decided by Wolbach's recent discovery of a Rickettsia body in the tissues.

In 1906 King definitely ascertained that the disease supervened on the bite of a certain tick, *Dermacentor venustus* (*D. andersoni*) (Figs. 68, 69), a discovery subsequently confirmed by Ricketts, who succeeded in conveying the infection to a monkey by means of an infected tick. McClintick in 1911, in researches conducted at the instance of the United States Government, failed to communicate the disease to guinea-pigs, but unfortunately himself contracted the infection and died. The most complete account yet published of this disease is the careful monograph of Wolbach of Harvard, in the *Journal of Medical Research*, 1919.

Geographical distribution.—The disease has been reported from several of the Western States of the American Union—Idaho, Montana, Wyoming, Utah, Nevada, Oregon, Colorado, and Washington State. It is believed to occur also in the Alaska Territory,

Digitized by Google

and in 1916 was definitely proved by Kelly and Cumming to exist in California. It is found principally in valleys and near the foothills of mountains in sharply defined and limited areas, and is confined to the spring months, the greatest number of cases occurring between March and July. It attacks any age, either sex, and is not directly contagious.

Symptoms.—A short period of malaise is followed by chills, which are repeated with diminishing severity at irregular intervals

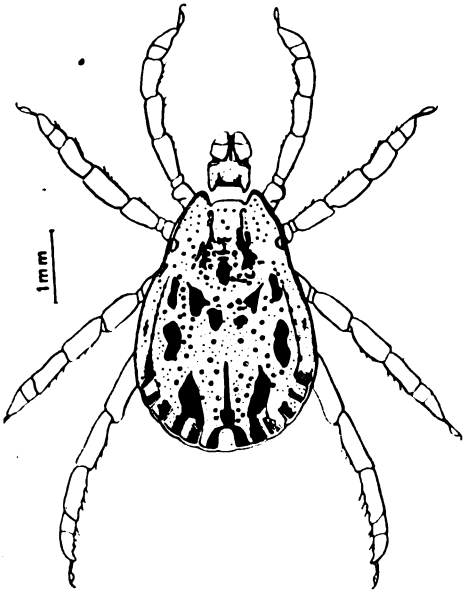


Fig. 68.—**Dermacentor venustus**, ♂. (*By courtesy of Prof. Nuttall.*)

throughout the attack. By the second day the temperature has risen to 103° or 104° F., and by the fifth day to 105° or 107°. A typhoid-like condition, with low muttering delirium and semi-consciousness, is rapidly developed. If the patient is to recover, the temperature begins to fall about the end of the second week; fever subsiding usually by lysis.

About the fourth to seventh day an eruption appears on the wrists, ankles, or back, extending rapidly to the trunk, scalp, hands, and feet. At first it consists of minute rose-coloured spots; these soon assume a petechial character and, spreading, tend to become confluent, especially on the more dependent parts of the body and limbs. In other instances the spots remain discrete,

Digitized by Google

brownish or purplish in colour, giving to the surface of the body a speckled appearance. A certain amount of icteric tinting of skin and scleræ is also present. During the third week desquamation sets in, the eruption fading as fever subsides. In some cases the skin of the elbows, fingers, toes, lobes of the ears, etc., becomes gangrenous.

Constipation is usual. The liver is slightly enlarged, the spleen markedly enlarged and tender. The scanty, high-coloured urine may contain albumen and casts. Early in all severe cases there is

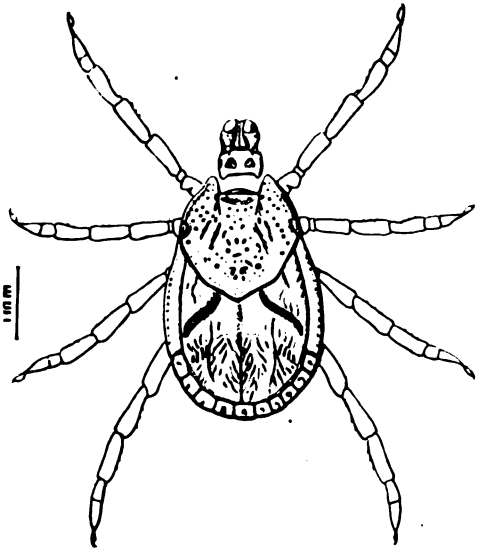


Fig. 69.—Dermacentor venustus, ♀. (*By courtesy of Prof. Nuttall.*)

œdema of the face and limbs. Nausea and vomiting set in about the beginning of the second week, and persist in fatal cases. Respiration is rapid. Slight catarrh of the respiratory tract is present throughout; the pulse loses in volume as it increases in frequency. There is but little diminution in the blood-count, and only a feeble leucocytosis—12,000 to 13,000; the hæmoglobin is slightly diminished.

Complications such as gangrene of the tonsils, scrotum, and prepuce are more common in the milder type of the disease, as seen in Idaho. One attack of the disease confers immunity, and no instance is known of a second attack of this fever in man.

Digitized by Google

Etiology.—The evidence is now conclusive that the germ of Rocky Mountain fever is introduced by the bites of *D. venustus*.* It is only the adult that attacks man. The Rocky Mountain goat, the domestic sheep, brown bear, coyote, badger, and wild cat also serve as hosts to the adult forms, but the larval and nymph stages develop principally on the ground-squirrel, *Citellus columbianus*, and the woodchuck, *Marmota flaviventer*, which have been shown by Ricketts to act as a reservoir of the virus, so that by feeding on these animals the tick becomes infected and capable of transmitting the disease to man. According to Wolbach's recent work, practically all small rodents of that region serve as hosts for the larvæ. The tick takes two years to develop, hibernating during the winter, feeding but languidly after the beginning of August, and reviving during the first warm days in April. It is possible that the Rocky Mountain goat also serves as a natural reservoir of the disease virus. It has been proved that various rodents in the endemic area—ground-squirrels, woodchucks, chipmucks, etc.—are susceptible to infection.

Wolbach (1918) has noted small bodies staining with Giemsa in the endothelial cells of the blood-vessels and in the testes of man and of guinea-pigs infected with the virus, as well as a very general distribution of these organisms in the bodies, salivary glands, and eggs of infected ticks (*Dermacentor*). Two morphological types are recognized: one a lanceolate diplococcal organism found in the circulating blood as well as in the endothelial cells, and containing chromatin staining substance; the other staining blue and rod-shaped. Frick has also found similar bodies within the red blood-corpuscles, as well as extracellular. These bodies, according to Arkwright, Bacot, and Duncan, resemble in many features the Rickettsia bodies found by them in the fæces of lice fed on typhus and trench-fever cases, as well as in the cells and lumen of the alimentary tract of these insects, but they are larger and more lanceolate. Wolbach proposes to call the parasite *Dermacentroxenus rickettsi*.

According to Ricketts, the germ will not pass through a Berkefeld filter and is intimately attached to the blood-corpuscles, is easily inoculated into man, and can be passed through an indefinite series of monkeys and guinea-pigs, giving rise in them to the characteristic symptoms, in which a scrotal swelling is held to be pathognomonic. In this manner immunity is produced. The

* The names *D. venustus* and *D. andersoni* refer to the same species. The differences in the nomenclature of the tick used by various authors have resulted in a good deal of confusion. *D. reticulatus* and *D. occidentalis*, apparently distinct species, have at various times been incriminated as carriers of the infection.

Digitized by Google

larva, nymph, and adult male and female tick are all of them efficient intermediaries for the parasite. Ricketts suggests—seeing that in one place (Montana) the case-mortality in man is as high as 90 per cent., whereas in another place (Idaho) it is only 5 per cent.—that there are two species of tick capable of carrying the infection; in the former instance it is *D. venustus*, in the latter *D. maturatus*. The proportion of infected ticks under natural conditions is small; only 1 in 296 in Ricketts' experience.

In conformity with the seasonal prevalence of the tick, the disease in man is commonest in April, May, and June.*

Pathology.—Post mortem, in addition to the skin lesions, there are marked hypostatic congestion of the lungs, subserous petechiæ, softened myocardium, enlarged firm spleen and lymphatic glands, fatty degeneration of the hepatic cells, and congestion of the cortex of the kidneys. Constant lesions, both in man and in animals, are hæmorrhages into the genitalia; gangrene of the prepuce and scrotum are often noted. Microscopically, proliferation of the endothelium of the arteries and veins of the skin and subcutaneous tissues, with accumulation of Rickettsia bodies, is seen, the cells taking on phagocytic properties and ultimately becoming necrotic. There is a perivascular mononuclear infiltration as in typhus.

Differential diagnosis.—The sudden onset, the joint pains, and the negative Widal reaction differentiate this fever from enteric; the geographical distribution and absence of Weil-Felix reaction serve to eliminate a possible diagnosis of typhus.

Treatment and prophylaxis.—In the absence of a specific remedy, treatment must be conducted on general principles, having regard to the natural history and character of the disease. Attempts at prophylaxis are now being carried out, based on the above-

* **Tick paralysis.**—According to Hadwen, the tick *D. venustus*, as it occurs in the dry district of British Columbia, Keremeos, gives rise to a peculiar form of paraplegia in sheep which, directly or indirectly, may prove fatal. In the same district it affects man and other animals in a similar way. Todd has called attention to this disease, of which he has collected a considerable number of cases, some of them fatal. Nuttall, working in Cambridge, England, has confirmed Hadwen's experiments. He placed one of the ticks received from Hadwen on a healthy dog. Twelve days afterwards the dog became completely paralysed in fore and hind legs. Ultimately it gradually recovered.

This form of tick disease is manifestly different from Rocky Mountain fever, as it is non-febrile, is unattended with eruption, and is not communicable by inoculation. Possibly it is produced by a poison instilled by the tick during haustellation. The wound it makes is very painful, is attended with œdema and, on forcible removal of the tick, with free bleeding as if some anticoagulin had been introduced. The symptoms of the disease suggest infantile paralysis.

In sheep the favourite points of attachment of the tick are on the back along the course of the spine; in man, the nape of the neck.

A somewhat similar form of paralysis is described by Eaton as following on tick bite in Queensland, Australia, the incriminated tick being *Ixodes ricinus*. Bancroft reports from the same country a similarly caused form of epileptiform convulsions in cats and dogs.

Digitized by Google

described mode of its transmission. War is being waged on the ground-squirrel and the woodchuck; domestic stock and goats are being systematically dipped to prevent the spread of and, if possible, to exterminate the tick.

Frick, finding that when *D. venustus* is placed on the fleece of an unshorn sheep it either dies or remains unimpregnated, and is manifestly on an uncongenial host, suggested, in addition to the measures just mentioned, turning the badly infected districts into sheep-runs.

Digitized by Google

CHAPTER XVII

JAPANESE RIVER FEVER

Synonyms. — Tsutsugamushi; Shimamushi; Kedani Mite Disease; Flood Fever; Batran, Mokkui, and Hovin Fevers; Pseudotyphus (Schüffner); Exanthematous Glandular Fever.

Definition.—An acute endemic disease running a definite course and attended with a considerable mortality, varying from 10 to 52 per cent. of those attacked. It is characterized by the presence on the skin of an initial eschar, supervening on the bite of a species of *Trombidium*. This is followed by an ulcer, lymphangitis, fever, an exanthematous eruption, bronchitis, and conjunctivitis.

History.—This disease was first described by Palm in 1878, and subsequently, more fully, by Baelz and Kawakami. Ancient records would indicate that the disease has been known for more than a thousand years.

Geographical and seasonal distribution.—Formerly it was thought that tsutsugamushi was confined to the banks of two rivers on the west side of the island of Nippon, Japan—the Shinanogawa and one of its tributaries, and the Omonagawa. Every spring these rivers inundate large tracts of country, and later in the year hemp is raised on strips of the inundated district. The crop is reaped in July and August, and it is solely among those engaged in harvesting and handling this that the disease occurs. It is not communicable by the sick to the healthy. Although transportable in the hemp to a very slight extent, it is only in limited spots here and there in the endemic districts that the virus originates. It now appears from the reports of Hatori that the disease is widely spread in Formosa, and possibly in Korea, both among the Japanese settlers and the aborigines. In Formosa it occurs in the highlands as well as in the coastal plains. It commences in April and disappears in November.

Ashburn and Craig have thought that a disease observed by them in the Philippines, as well as by Schüffner in Sumatra, is possibly identical with the Japanese fever, as may also be the Mossman fever amongst the cane cutters of Queensland, described by Smithson in 1910.

Etiology.—The Japanese attribute this disease to the bite of a

Digitized by Google

larval acarus (locally called *akamushi*—red insect), *Trombidium akamushi*, resembling the *Leptus autumnalis* of Europe, and popularly known as the kedani mite or "patau" (Fig. 70). Men, women, and children are equally susceptible; on account of their occupation it is commoner in men. New arrivals in the endemic districts are said to be more liable to the disease. One attack does not confer immunity, although it may render subsequent attacks less severe. As yet the virus of the disease, which doubtless enters in the first instance at the site of the primary eschar, has not been finally determined. Hayashi has found rod-like bodies staining with

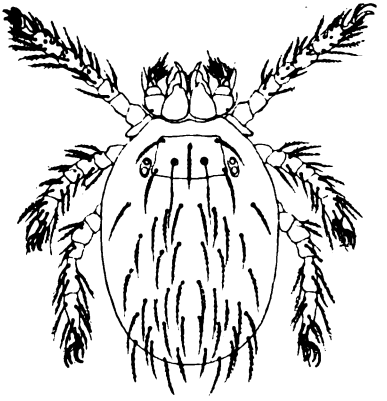


Fig. 70.—Microtrombidium akamushi, Brumpt: larva of T. akamushi. × 100. (*After Hirst, "Journ. Economic Biol."*)

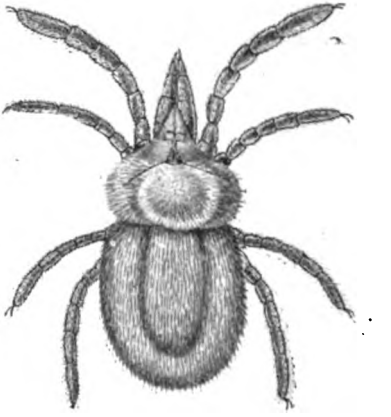


Fig. 71.—Trombicula akamushi: full-grown imago. × 35. (*After Miyajima and Okumura.*)

Giemsa in cells of lymphatic glands and the spleen, morphologically like those of East Coast fever in cattle. Blood from infected cases injected into rats, monkeys, and marmosets conveyed the disease to these animals, and the parasite could be demonstrated in their tissues as well as in other animals inoculated with an emulsion of trombidia. Mizayima states that tsutsugamushi is communicable to the monkey by the bite of the insect, and also by inoculation from a human patient.

According to Kawamura and his co-workers, the blood of patients is very infective in the incubation period of the disease. The minimum dose capable of infecting monkeys is 0·001 c.c. The infective agent is easily destroyed by heating at 50° C. for ten minutes. The mite occurs in large numbers on the ears of

Digitized by Google

field-mice and other rodents, which, however, have not been found to be suffering from any particular disease at the time. It has recently been pointed out that this mite is widely distributed by the agency of a small warbler, *Acrocephalus orientalis*. Its life-cycle has now been worked out by Nagayo, Kawamura, and others, and it is known to be the hexapod larva of *Trombicula akamushi*, a red mite measuring 0·9 mm. in length, which is non-parasitic in its habits but lives in grass (Fig. 71). Recent work suggests that the virus of tsutsugamushi also exists in the body cavity of the adult mite.

Symptoms.—After an incubation period of from four to ten days the disease usually begins with malaise, frontal and temporal headache, anorexia, chills alternating with flushes of heat, and prostration. Presently the patient becomes conscious of pain and tenderness in the lymphatic glands of the groin, armpit, or neck. On inspection of the skin of the corresponding lymphatic area there is discovered—usually about the genitals or armpits—a small (2 to 4 mm.) round, dark, tough, firmly adherent eschar surrounded by a painless livid red areola of superficial congestion. Occasionally two or three such eschars are discovered. Although a line of tenderness may be traced from the sore to the swollen, hard, and sensitive glands, no well-defined cord of lymphangitis can be made out. The superficial lymphatic glands of the rest of the body, especially those on the opposite side corresponding to the glands primarily affected, are also, but more slightly, enlarged.

Fever of a more or less continued type now sets in, the thermometer mounting in the course of five or six days to 104° or 105° F. The conjunctivæ become injected, and the eyes somewhat prominent; at the same time a considerable bronchitis gives rise to harassing cough. The pulse is full and strong, ranging rather low—80 to 100—for the degree of fever present. The spleen is moderately but distinctly enlarged, and there is marked constipation.

About the sixth or seventh day an eruption of large dark-red papules appears on the face, tending to become confluent on the cheeks, and fading on pressure. It then extends to the forearms, legs, and trunk, being less pronounced on the upper arms, thighs, neck, and palate. Simultaneously with the papules a minute lichenous eruption breaks out on the forearms and trunk. This lasts usually from four to seven days; if but slightly marked the eruption may fade in twenty-four hours, the site being marked by pigmentation.

The patients during the height of the fever are flushed, and at

Digitized by Google

night, it may be, delirious. They complain incessantly, probably on account of a general hyperæsthesia of skin and muscles. Deafness is also a feature.

As the disease advances, the symptoms become more urgent; the conjunctivitis is intensified, the cough becomes incessant, the tongue dries, the lips crack and bleed, and there may be from time to time profuse perspiration. By the end of the second week—sooner or later according to the severity of the case—the fever begins to remit, the tongue to clean, and, after a few days, temperature falls to normal and the patient speedily convalesces. There is a well-marked leucopenia. The red cells are normal, but there is a decrease of the coagulability of the blood. Bronchitis, diarrhœa, or diuresis may occur during the decline of the fever. The circular, sharp-edged, deep ulcer left after the separation of the primary eschar—an event which usually takes place during the second week—now begins to heal, and the enlargement of the glands gradually to subside. The urine is albuminous and gives the diazo-reaction.

Such is the course of a moderately severe case. In some instances, however, the constitutional disturbance is very slight, although the primary eschar may be well marked and perhaps extensive. On the other hand, the fever may be much more violent, and complications such as parotitis, melæna, coma, mania, cardiac failure, or œdema of the lungs may end in death. Similarly, the duration of the disease varies according to severity from one to four weeks, three weeks being about the average. Relapses do not occur.

Pregnant women contracting tsutsugamushi mostly abort and die.

According to Hatori, reinfection may occur.

Pathological anatomy. — Beyond evidences of bronchial catarrh, hypostatic pneumonia, enlarged spleen, perisplenitis, patchy reddening of the intestine near the ileo-cæcal valve, injection of the peritoneum, and slight enlargement of the mesenteric and superficial lymphatic glands, no noteworthy lesions have been described.

Differential diagnosis.—The limited geographical distribution and seasonal incidence of the disease, together with the initial necrotic ulcer and lymphadenitis, should prevent any error in diagnosis. Plague may possibly be thought of in the first instance, but, even if a primary vesicle or ulcer exists in this disease, the matting together and exquisite tenderness of the lymphatic glands should put one on one's guard. Typhus, measles, and dengue may also be thought of.

Digitized by Google

Treatment.—The site of the bite should be treated by cauterization or extirpation. Hayashi and Mukoyama have employed the serum of cattle and monkeys which have recovered from the disease, therapeutically. In severe cases in which it was injected in the early stages of the disease, successful results were obtained. Salvarsan has been found to be useless. The remainder of the treatment is symptomatic only.

Prophylaxis.—All parts of the body in a mite-infested country should be properly protected. For this purpose a mite-proof suit has been devised by Hayashi and Nagayo. All articles of clothing used in infested fields should be sterilized and the parts of the body exposed to mite-bites bathed with Vleminck's solution. The most effective measure is the burning down of the bushes and grass in the endemic area before bringing it under cultivation.

Digitized by Google

CHAPTER XVIII

TYPHUS FEVER IN THE TROPICS

Synonyms.—Typhus Exanthemicus ; Tarbadillo (Mexico) ; Brill's Disease.

Definition.—An acute specific fever, of abrupt onset, followed by pyrexia of a remittent type of fourteen days' duration, terminating generally by crisis. On or about the fifth day there appears a roseolar eruption tending to become petechial and spreading from the abdomen over the trunk and extremities. The virus is conveyed by lice.

Geographical distribution.—Typhus has been eradicated in peace times from most civilized European countries, but reappears in times of stress and famine in epidemic form, as in the recent war. In certain subtropical countries, as in North Africa, the disease is widespread among the poorer natives. In the equatorial regions it is rare, but is found in India at the higher elevations, and a particularly virulent form is met with in Mexico, where it is known as "tarbadillo."

Etiology.—Typhus is conveyed by lice (*Pediculus corporis* and *P. capitis*) ; the virus is filterable and infective for monkeys and guinea-pigs ; it is present in the blood-plasma during the first five days of the disease. A developmental cycle would appear to take place in the body cavity of the louse, which is infective only from the fourth to the seventh day after a meal of typhus blood. Infection is conveyed through the fæces of the louse, and is inoculated by scratching. Recent work by Arkwright points to a minute organism, the *Rickettsia prowazekii*, which is found in the body of the louse, as being possibly the infecting virus. Similar bodies have been found in trench-fever lice and in *Dermacentor venustus*, the tick of Rocky Mountain fever. The important discoveries in Poland of the Typhus Fever Commission of the League of Red Cross Societies (Wolbach and Todd) have furnished additional evidence that the Rickettsia must be regarded as the infecting agent. They have found small rod-like bodies staining with Giemsa, generally occurring in pairs, about 0·5 μ in length, in the phagocytic endothelial cells of the blood-vessels in the skin, testes, and brain. They are similar to the Rickettsia bodies found in the intestinal cells

Digitized by Google

of infected lice. These workers have proved that injection of the intestines of lice containing these rod-like bodies into guinea-pigs produces an acute illness with consequent characteristic lesions.

The Rickettsia bodies of typhus are said to differ morphologically from those of trench fever, and are intracellular, while those of the latter disease are extracellular.

Morbid anatomy and pathology.—The blood is dark-coloured and does not clot; the liver and kidneys show cloudy swelling. There is generally a moderate enlargement of the spleen, with hyperplasia of the lymph-follicles; the substance is soft and diffluent. Bronchial catarrh is generally present, with hypostatic congestion of the lungs. There are no changes in Peyer's patches, and the mesenteric glands are not affected, typhus being thus differentiated from typhoid fever. The eruption is due to a localized necrosis of the walls of the smaller blood-vessels, with local collections of lymphocytes and plasma cells in the adventitia. These nodules, which are characteristic, are found in the brain and other viscera, as well as in the skin. The essential lesions are due to a phagocytosis by the vascular endothelium which is followed by necrosis of these cells.

Symptoms.—The incubation period varies between four and fourteen days, twelve being the average. The period of onset lasts about two days, during which time the patient may experience headache, nausea, giddiness, etc. Occasionally in fulminating cases general convulsions occur, passing into delirium. On the third day the temperature rises suddenly to 103° or 104° F., the face becoming congested, the eyes suffused. (Chart 11.) There is a peculiar stuporose, drunken look such as is not found in any other disease—except, possibly, plague. The mouth becomes foul, the tongue coated with dense brown fur, the breath offensive. Epistaxis is frequent in some epidemics, and vomiting may be a distressing feature. The temperature remains raised, with slight morning remissions, for the next twelve or fourteen days. The urine shows a slight cloud of albumen, as a rule, the urea and chlorides are increased in amount.

The rash appears on the fifth day, first upon the abdomen and inner aspect of the arms, spreading over the chest, back, and trunk, rarely involving the face; it is generally pleomorphic. The term "mulberry rash" has been used to describe the features of the exanthem, but it really consists of roseolar macules, together with a fine irregular dusky mottling below the epidermis, generally known as "subcuticular mottling"; it may become petechial and

Digitized by Google

involve palms of hands and soles of feet. Exceptionally, however, the rash, instead of being a mixture of purple and copper, is bright red in colour; it may be hæmorrhagic. It fades slowly, and may be visible altogether for ten days. After the appearance of the rash, prostration and cardiac weakness become pronounced.

In brown or dark-skinned natives a typhus rash may be very difficult to discern; to make the subcuticular mottling visible, thorough cleansing of the skin and placing the patient in a good strong light are often necessary. Congestion of the arm by means of a tourniquet on the upper part may render the petechial spots more distinct, and has been practised with success in the

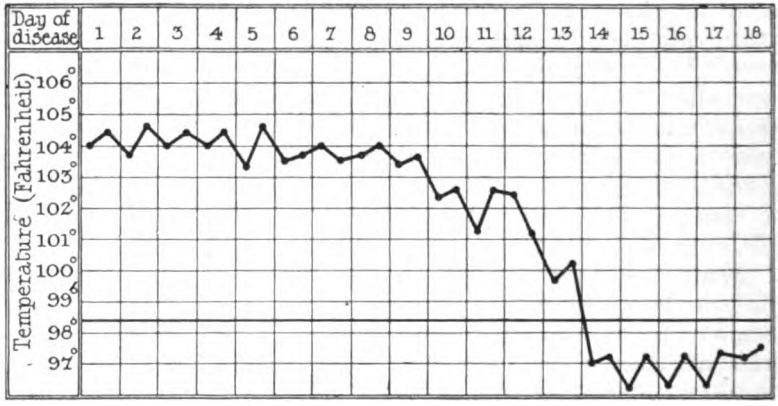


Chart 11.—Typhus fever. (*Orig.*)

early diagnosis of the rash in Europeans. In natives the region round the umbilicus often shows the rash in its most pronounced form.

When a typhus epidemic attacks an isolated population, as for instance in a desert oasis, terrible complications due to sepsis and neglect may ensue; in such circumstances a terminal broncho-pneumonia is very common. In the survivors from an attack there may be extreme emaciation as well as implication of the nervous system, manifesting itself as ataxia, violent tremors, mania or dementia. Abortion in pregnant women is common. The young and the aged readily succumb. Parotitis is a frequent complication. Relapsing fever and typhus may frequently co-exist. Constipation rather than diarrhœa is the rule, the mouth becoming very foul, and the lips and teeth being covered with sordes. Bedsores are a frequent complication.

Digitized by Google

Together with the appearance of the rash there may be signs of bronchitis, the mental lethargy becomes more pronounced, the patient sinking into the "typhus" state. His cerebration is low, his hands and tongue are tremulous; he is difficult to nurse, and emits a peculiar odour which has been compared to "gun-washings," or that emanating from a cupboard containing well-blacked boots. Amongst so many malodorous emanations the peculiar aroma said to be characteristic of typhus fever may not always be distinguishable. In the second week a low muttering delirium supervenes, and the secretion of urine may be diminished or even suppressed. The spleen may be enlarged. Often symptoms of cortical irritation, such as muscular twitchings and incontinence of urine, may be observed.

As the fourteenth day approaches, signs of an improvement set in and the temperature may suddenly fall by crisis, or more generally in tropical cases by a rapid lysis. If a fatal issue is to ensue it generally occurs about the twelfth or fourteenth day, or may be later, when the temperature is subnormal, from exhaustion or cardiac failure.

During convalescence the greatest care should be taken against excitation of the heart of any kind.

Mild cases of typhus, in which the rash rarely becomes purpuric, often occur sporadically, and in fact are almost constantly to be met with in the endemic areas in the subtropics. In America they have been known as Brill's disease. The blood picture shows nothing definite, though there is said to be a moderate leucocytosis of 12,000 to 15,000.

Diagnosis.—Typhus in the early stages is apt to be confused with enteric, relapsing, or cerebro-spinal fever, or with subtertian malaria. During an epidemic there is rarely any doubt. The more gradual onset of the fever and the less marked stuporose condition, together with a negative hæmoculture, differentiate enteric from it. The other conditions mentioned which may simulate typhus may be readily differentiated by laboratory diagnosis. It is said that plague presents the same picture of alcoholic intoxication as does typhus, but in the former there is no rash. Influenza of acute onset, such as the epidemic of 1918, may simulate typhus in its early stages. The rashes of Japanese river fever and of the spotted fever of the Rocky Mountains have many features in common with typhus, but difficulty in diagnosis is liable to arise only in the restricted areas in which those fevers occur.

The Weil-Felix reaction, first discovered by Wilson of Belfast, is a very real aid to diagnosis in typhus. A bacillus, *Proteus vulgaris*,

Digitized by Google

now termed X 19, and originally isolated from the urine, where undoubtedly it occurs only as a contamination, possesses in emulsion the extraordinary property of being agglutinated by typhus serum as early as on the fifth day of the disease. The test may be performed in test-tubes by the progressive dilution method (p. 897), or with Garrow's agglutinometer. By the latter method an agglutination of 1 : 20 may be regarded as diagnostic. The maximum agglutination results are obtained from the eighth to the twenty-first-day; a titre of 1 : 2,500 has been recorded; the reaction may be obtainable for sixty days. Occasionally typhus serum may agglutinate cultures of *B. typhosus* as well.

The appearance of this specific agglutinin in the blood of typhus cases is not accompanied by the formation of specific immune bodies, as has been shown by Fairley, though the latter are produced when a normal person is injected with cultures of X 19. Using an emulsion of this organism as an antigen, a positive complement-deviation reaction may be obtained with the serum of such a person.

There is little evidence, either from systematic blood and urine cultures during life, or from the organs post mortem, that this bacillus (*P. vulgaris*), which can be cultivated in artificial media with ease, is the etiological factor in typhus.

Treatment.—As there is no specific drug in typhus, special care must be devoted to nursing. Strict attention must be paid to the hygiene of the mouth. The recumbent position is absolutely essential. It is equally essential that the patient have as much fresh air as is possible. Stimulants must be given to maintain the cardiac action, the favourite being port wine; but care must be exercised that it is not given, as is so often the case, in excess—8 oz. in the twenty-four hours is sufficient. Digitalis or digitalin ($\frac{1}{100}$ gr.) is indicated as a cardiac stimulant. Lumbar puncture may be employed to relieve the delirium and other cerebral symptoms; as a rule there is excess of pressure in the cerebro-spinal fluid. There are no special precautions with regard to diet, which should be nutritious and easily digestible.

Prophylaxis.—This consists almost exclusively in the destruction of body lice. The body should be shaved—including the pubes and axillæ—and the hair of the head cropped. After a cresol bath the underclothing should be smeared with a preparation consisting of unwhipped naphthaline 4 parts, soft soap 1 part; but whenever possible all clothing, including blankets and bedclothing, should be disinfected, preferably by dry heat. To kill lice and their eggs with certainty a temperature of 55° C. for 30 minutes,

Digitized by Google

or of 60° C. for 15 minutes, is required. Disinfestation of clothes on a large scale may be accomplished on the railway in luggage vans, by closing the doors and turning on superheated steam from the engine. The use under field conditions of the Serbian barrel, in which the clothes are saturated with steam under pressure from water within the barrel itself, is a practical method. In default of steam, ironing of the seams of the clothing has been found useful. Soaking in 2-per-cent. lysol destroys both the pediculi and their eggs.

Digitized by Google

CHAPTER XIX

PLAGUE

Definition.—Plague is a specific, inoculable, and otherwise communicable epidemic disease common to man and many of the lower animals. It is characterized by fever, adenitis, a rapid course, a very high mortality, and the presence of a specific bacterium, *Bacillus pestis*, in the lymphatic glands, viscera, and blood. In a large proportion of cases buboes form in the groins, armpits, or neck.

Geographical distribution.—Though not necessarily confined to warm climates, in modern times plague, like leprosy, has practically become so. The hygienic conditions which advancing civilization has brought in its train have forced back these two diseases from Europe, where at one time they were even more prevalent than they are in their present tropical and subtropical haunts. Plague and leprosy are typical examples of that large group of acute and chronic germ diseases whose spread depends on social and hygienic rather than on climatic conditions, and more especially on the verminous accompaniments of filth and overcrowding; conditions which nowadays are found, to an extent and with an intensity sufficient to ensure the endemic prevalence or epidemic extension of these diseases, for the most part only in warm countries.

The first authentic account of plague in Europe relates to an outbreak in A.D. 542, which, starting from Egypt, spread over the Roman Empire. The disease visited England as a widespread epidemic for the last time in 1664–79, and in 1664–5 upwards of 70,000 out of the 460,000 inhabitants of the London of that day perished. From that time until 1841, when plague appeared for the last time in Constantinople, it recurred again and again in different parts of Europe. In 1878–9 a small epidemic, which speedily died down, broke out in the Russian province of Astrakhan. With the latter exception and the limited epidemics at Oporto in 1899 and at Glasgow in 1901, and a few isolated and mostly imported cases at large seaports, Europe has long enjoyed exemption from this worst of epidemic diseases. In recent years and from time to time cases of plague have occurred in the Port of London in seamen from Eastern countries, and plague-infected rats are by no means

Digitized by Google

uncommon in the docks of the metropolis, but, with the exception of a limited epizootic in rats and rabbits and several fatal cases in man in 1910 in Suffolk, there is no record of plague in England, apart from the cases occasionally seen in the seaports, since the seventeenth century.

Probably plague is always present in some part of India, especially among the rude hill-peoples. It is known to have been endemic in the south-west of China, in the province of Yunnan, for many years. The present extension of plague probably had its origin in that part of China. There it was seen by Rocher and others in 1878 and afterwards. It is safe to prophesy that plague will continue epidemic in that country for many years to come. Japan and the Philippines were both infected from China.

Having probably been imported from Hong Kong, it appeared in 1896 at Bombay, and subsequently as a great epidemic spread to Calcutta and to many other parts of India, where it still prevails. The mortality from the current epidemic is numbered in millions.

Soon after its appearance in India, plague became extensively epidemic in Mauritius, where it still prevails at certain seasons. Mombasa and British East Africa (including Nairobi), the West African colonies, Madagascar, Delagoa Bay, Cape Town, Port Elizabeth in Cape Colony, and Durban; also Sydney and Brisbane in Australia, and Alexandria in Egypt, have all been invaded.

Until its recent appearance in Brazil, the Argentine, and other South American countries, and in San Francisco and Mexico, plague has never invaded the Western hemisphere.

ETIOLOGY

The micro-organism.—The proofs are now complete that the specific cause of plague is the cocco-bacillus which was discovered first by Kitasato, and afterwards independently by Yersin, during the Hong Kong epidemic in 1894. This microbe occurs in great profusion in the characteristic buboes—generally in pure culture, although towards the later stages it is often associated with the streptococci and staphylococci of suppuration. It is present, besides, in great abundance in the spleen, intestines, lungs, kidneys, liver, and other viscera, and also, though in smaller numbers, in the blood. In the pneumonic type of the disease it is present in the expectoration in enormous numbers. It occurs also in the urine and fæces; in the latter, though detectable by inoculation and by cultivation, the bacillus may be hard to find by direct observation. Towards the termination of rapidly fatal cases it may become so

Digitized by Google

abundant in the blood as to be readily observed there with the microscope.

The plague bacillus (Fig. 72), as seen in a blood-film, or in smearings or scrapings from the pulp of the buboes, or from any of the inflamed lymphatic glands, or from the viscera, is a short, thick cocco-bacillus (1·5 to 2 μ and 0·5 to 0·7 μ) with rounded ends, very like that of chicken cholera. A capsule, according to Gordon, or the appearance of a capsule, can generally be made out, especially in those bacilli which are present in the blood. The bacillus is readily stained by aniline dyes, especially with Romanowsky

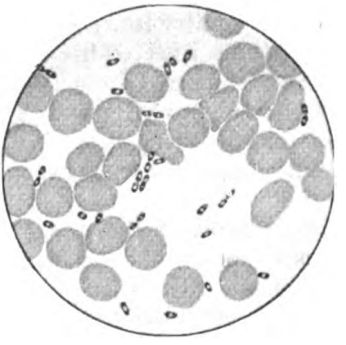


Fig. 72.—B. pestis in peripheral blood in septicæmic plague. × 500. (*Microphoto: Dr. J. Bell.*)

stains, the extremities taking on a deeper colour than the interpolar part, giving it a bipolar appearance. It is usually decolorized by Gram.

Culture characters.—When sown on blood serum and kept at body temperature, in from twenty-four to forty-eight hours an abundant moist, yellowish-grey growth is formed without liquefaction of the culture medium. On agar, but better on glycerin agar, the growths have a greyish-white appearance. In agar plate cultures they show a bluish translucence, the individual colonies being circular, with slightly irregular contours and a moist surface; on mannite neutral-red-bile-salt agar the colonies are bright red, but are colourless on a similar medium in which lactose is substituted. Litmus-milk and glucose-broth are rendered slightly acid, lactose-broth is unchanged. Young colonies are glass-like, but older colonies are thick at the centre and more opaque; they are singularly coherent and may be removed *en bloc* with a platinum needle. Stab cultures show after one or two days a fine dust-like line of growth. According to Yersin, when sown on gelatin the bacillus gives rise to white transparent colonies which, when examined in reflected light, present iridescent borders. In bouillon the cultures present a characteristic appearance: the liquid remains clear, whilst a granular deposit takes place on the sides and bottom of the tube Cultivated on broth in which clarified butter or coco-nut oil is floated, *B*

Digitized by Google

pestis presents characteristic stalactite growths which gradually fall off, forming a granular deposit. Examined with the microscope, these various cultures show chains of a short bacillus, presenting here and there large bulbous swellings. In gelatin the bacilli sometimes form fine threads, sometimes thick bundles made up of many laterally agglomerated bacteria, and involution forms are common. The bacillus does not produce spores.

The most favourable temperature for culture is from 36° to 39° C.

Intensification and attenuation of virus.—There can be no question that, both by artificial means and in a natural way, the virulence of the bacillus of plague is susceptible of modification. It is known that in some instances the virulence and case-mortality of a plague epidemic show a tendency to decrease, the early cases being the most frequently and most rapidly fatal.

Recent observations in India have brought to light a form of chronic plague in rats, in which the specific bacterium, without seriously affecting the health of the animal, remains latent for long periods in abscesses in connection with spleen, liver, or abdominal lymphatics. Although thus latent, it is potentially virulent, proving lethal when cultures obtained from these abscesses are injected into other animals. These facts seem to indicate that under certain unknown natural conditions the virus tends to acquire increased potency, whilst in other circumstances its virulence tends to diminish.

This conjecture is countenanced by the results of experiment on animals. It has been shown that by passing the virus by inoculation from one guinea-pig to another the rate of its action becomes accelerated. On the other hand, Yersin found that certain rapidly developing colonies of the bacillus possessed a diminished virulence, and that if these rapidly growing cultures are frequently repeated, in the long run they cease to be fatal to guinea-pigs, although they may still prove fatal to white mice. These data led up to Yersin's application to man of a prophylactic inoculation against plague.

The gravity of an attack of plague is not affected by the *amount* of virus introduced. Barber, using an ingenious apparatus, infected guinea-pigs, each with a single bacillus. The resulting disease was just as fatal as that produced by an injection of 500 bacilli.

Experimental plague. *Inoculation.*—Intentional and unintentional experiments have proved the inoculability of plague in man. Whyte in 1802 communicated the disease to himself, and died of it. At Cairo, in 1835, two condemned criminals were inoculated from the blood of plague patients; they contracted the disease, but recovered. The deplorable accident in a Vienna

Digitized by Google

laboratory, in October, 1898, by which fatal plague of a pneumonic type was acquired—in what way is not exactly known—from manipulations with plague cultures, goes far to complete the little that was wanting in the chain of evidence that this disease is caused by the introduction of the specific bacillus into the human body. The unintentional experiment in this instance, at all events, was not vitiated by having been made in the presence of a plague epidemic.

There is no reason for supposing that man differs in this respect from the lower animals, many of which are exceedingly susceptible to inoculation. Mice, rats, guinea-pigs, and rabbits are invariably killed if successfully inoculated from the buboes* of plague patients.

In the case of the guinea-pig, within a few hours of the introduction of the virus a considerable amount of œdema is already apparent around the puncture, and the adjacent gland is perceptibly swollen. At the end of twenty-four hours the animal is very ill; its coat is rough and staring, and it refuses food. Presently it falls on its side and becomes convulsed, one fit following another with increasing frequency as death approaches. If the body is opened immediately after death a rosy-red sanguineous œdema is found at the point of inoculation, with hæmorrhagic inflammatory effusions around the nearest lymphatic gland, which is much swollen and full of bacilli. The intestines are hyperæmic; the adrenals, kidneys, and liver are red and swollen. The much-enlarged spleen frequently presents an eruption of small whitish granulations resembling in appearance miliary tubercles. All the organs, and even any serous fluid that may be present in peritoneum or pleura, will be found to contain plague bacilli. In the blood, besides those free in the liquor sanguinis, bacilli are to be found in the mononuclear, though not, it is said, in the polynuclear leucocytes.

Feeding experiments.—Rats, mice, monkeys, birds, cattle, and pigs fed on cultures of plague bacilli, or on fragments of the liver or spleen of animals dead of plague, acquire the disease, and generally die with the characteristic symptoms and lesions. The disease thus induced may be either of an acute or of a chronic nature. When the latter, it may be ill defined and not easily recognized. Thus, pigs may show no marked signs of illness until a month after feeding on infective material, and then only a few days or hours before death.

Rôle of the rat in plague.—Although small and circum-

* The pus from a bubo is not always infective. Inoculation made with it may fail. Apparently the bacteria of suppuration may kill out the *Bacillus pestis*.

Digitized by Google

scribed epidemics of plague may occur without the intervention of the rat, as for instance in the recent outbreak in Colombo, there can be no doubt that in most epidemics of the bubonic form this rodent plays an important part both in the introduction and in the spread of infection. The species principally concerned are *Rattus norvegicus* (or *decumanus*)—the grey rat, and *Rattus rattus*—the black rat (Figs. 73, 74). The bandicoot and musk rat are of little importance in these respects, although susceptible to the infection. In Bombay the epizootic appears first in the *Rattus norvegicus* community, *Rattus rattus*—the more domestic species—being sub-

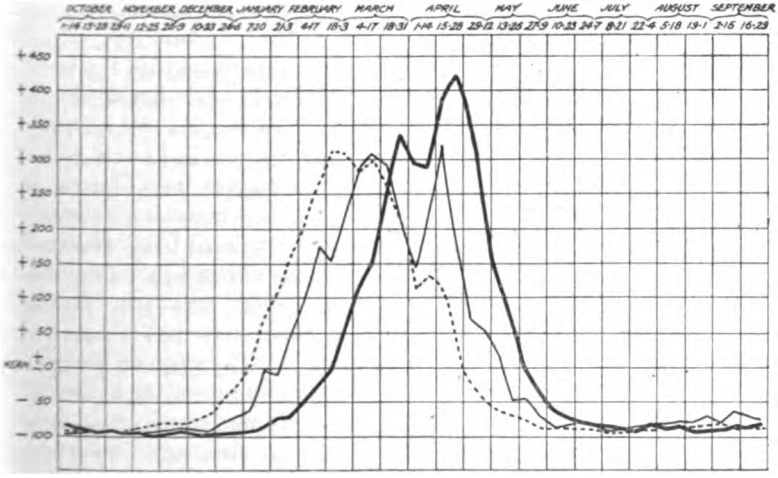


Chart 12, showing progress of plague in rats and man. (*From Report of Indian Plague Commission.*)

..... Infected *R. norvegicus*.
— — Infected *R. rattus*.
——— Human deaths from plague.

sequently attacked. Later the disease appears in epidemic form in man. (Chart 12.)

The seasonal prevalence of bubonic plague in rats is marked, and is not due to a periodicity in their reproduction, but is connected with periods in which fleas are most numerous.

The ancients were well aware of the connection between plague and the rat. In the Bible the rat is mentioned in association with the plague which broke out among the Philistines after they stole the Ark of the Covenant. Sambon describes a coin of Lucius Severus at the time of a great plague epidemic. On the coin is the god of medicine, Æsculapius, having at his feet a dead rat and at

Digitized by Google

his side a naked human figure in an attitude of terror or supplication. Many modern observers also have remarked the great mortality among rats and other animals which generally precedes and accompanies outbreaks of plague in man.

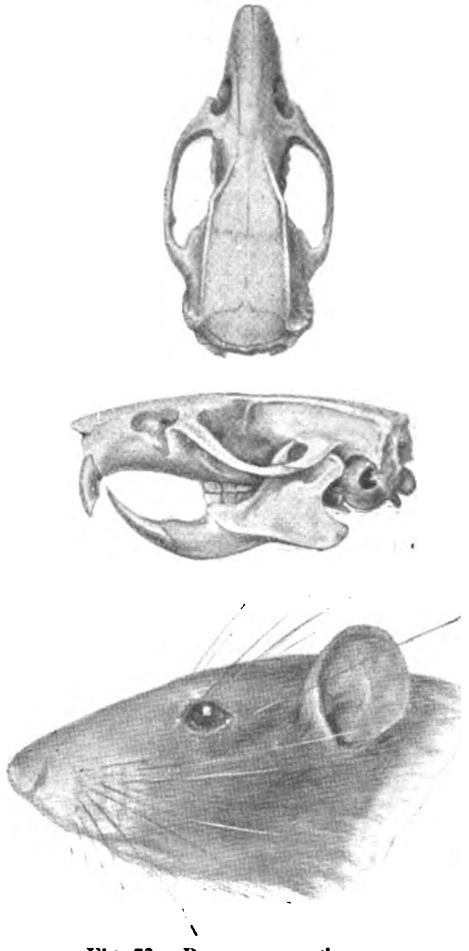


Fig. 73.—Rattus norvegicus.
Configuration and anatomical characters of head and skull (nat. size).

Glen Liston states that in places in which plague epidemics keep recurring year after year the local rats acquire a considerable degree of immunity, and, moreover, that this immunity is transmitted hereditarily. Thus in plague-free towns in India—e.g. Madras and Dacca—the mortality among the local black rats experimentally infected was 100 per cent., while in plague-stricken towns such as Cawnpore and Poona it was much less.

Another observation, already referred to, which together with the foregoing may have important bearings on the spread of plague and the yearly recurrence of epidemics in the same place, is that in certain rats the disease may assume a chronic form. Rats have been known to quit villages in anticipation of the advent of the disease.

Other animals may die of plague during an epidemic; oxen, sheep, deer, pigs, and dogs are all attacked at times, the dog less severely and less frequently.

Digitized by Google

Rôle of the marmot and other rodents.—Clemow has pointed out the connection of Mongolian and Siberian plague epidemics with the occurrence of the disease in a species of marmot called tarbagan (*Arctomys bobac*), common and much hunted in those regions (Fig. 75). This animal can harbour the plague bacillus in its body without apparently suffering any ill effects during hibernation, thus constituting a more or less permanent reservoir of the plague virus.

The ground-squirrel of the Caucasus (*Spermophilus guttatus*) is extremely susceptible to plague infection, and is probably concerned in the spread of the disease in that region. In California the ground-squirrel (*Citellus beechyi*, Fig. 76), although it does not live near human habitations, infects rats that do, and thereby acts as an important reservoir of *B. pestis*. It has been ascertained that in this instance the flea *Ceratophyllus acutus*, which infests both animals, acts as the carrier of the plague bacillus from one to the other, the infection being ultimately transmitted to man by the rat-flea (*Xenopsylla cheopis*).

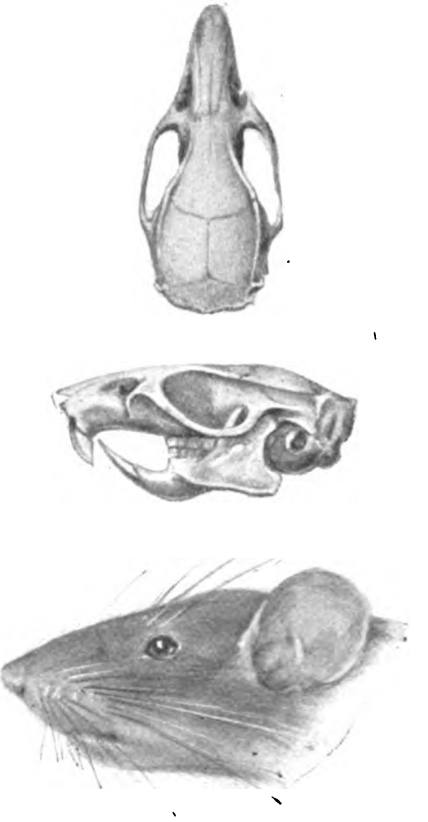


Fig. 74.—Rattus rattus.
Configuration and anatomical characters of head and skull (nat. size).

These and many similar facts observed in Bombay, Sydney, Cape Town, Hong Kong and elsewhere with regard to plague in the lower animals throw important light on one of the ways in which the disease is spread. They, together with the results of the several experiments already alluded to, have to be reckoned with in the future, more than they have been in the past, in devising schemes of quarantine,

Digitized by Google

and also in attempts at stamping out the disease in already affected localities. The wholesale destruction of domestic vermin should go hand in hand with the isolation of plague-stricken patients.*

Rôle of the flea in plague.—Yersin's original experiment on the carriage of plague by fleas has been successfully repeated again and again on mice, rats, guinea-pigs, and monkeys, and with many modifications. The result has been indisputable confirmation of the theory that bubonic plague is not communicable from animal to animal by simple contact, but that it is readily communicated by ectozoa, especially rat-fleas—principally *Xenopsylla cheopis* (Fig. 77), the rat-flea of the tropics, and *Ceratophyllus fasciatus*, the rat-flea of temperate climates—which act as passive intermediaries and carriers of the bacillus. The *Bacillus pestis* multiplies in the stomach of the flea, and retains its virulence for over twenty days, and is then passed out in the fæces; so that the flea serves not only as a carrier, but also as a multiplier of the germs.

Fig. 75.—Arctomys bobac, Siberian marmot. Nat. size.

Especially convincing are the experiments of the Indian Plague

* It is stated that the handling of a rat newly dead of plague is fraught with danger, whereas a rat that has been dead for some time and is cold and stiff may be touched with impunity; and it is surmised that the fleas of the newly dead rat are still in its fur, and quit it for the body of the manipulator, carrying on their probosces the bacilli of the disease, which they introduce when they proceed to feed on their new host. When a rat has been dead for some time and the body is cold, the fleas have already forsaken it—hence the impunity with which the rat itself may be handled; but the danger of infection remains in the locality in which it died and where the hungry infected fleas are awaiting an opportunity for a meal. The fact that in man the glands of the legs are usually the first to become implicated in the majority of cases of plague suggests that the virus is generally introduced through the skin of the feet or legs, which are just those parts most likely to be attacked by a flea picked up in walking across the floor of a room in which plague-stricken rats or other animals have died.

Plague epizootics occur in mice, but are not associated with plague in man. *Ctenopsylla musculi*, the mouse-flea, does not readily feed on man. The human flea, *Pulex irritans*, may transmit *B. pestis* under experimental conditions, yet it plays little or no part in the natural spread of the disease.

Digitized by Google

Commission, which clearly show that if fleas are excluded healthy rats will not contract the disease, even if kept in intimate association with plague-infected rats. Young rats may even be suckled by their plague-stricken mothers and remain healthy. But if fleas are introduced, whether naturally or intentionally, into the field of experiment, plague at once begins to spread from rat to rat, and with a rapidity in proportion to the number of fleas present. The Commission has shown further that an epizootic of rat plague may start without contact or even proximity of healthy and infected animals. It suffices to transfer fleas from a plague animal on to a healthy animal, or to place the latter in a room in which plague rats have died recently and been subsequently removed. The fleas that have left the body of the dead rats, remaining in the room, convey the germs. The atmosphere of the room is not infective; for if the experimental animal be suspended in an open cage a few feet above the floor it does not become infected. Nor is the animal infected if placed on the floor, if the precaution be taken to surround the cage with "tangle foot" so as to keep off the fleas. But if it be placed on the unguarded floor, either in its cage or allowed to run about, or even if it be suspended two inches above the floor —a distance not beyond the saltatory powers of the flea—it will become infected. The Commission obtained practically the same results in experiments with guinea-pigs in plague-infected houses. It is therefore no longer open to question that the important —probably the most important—agents in the development and perpetuation of plague epidemics are the rat and the rat-flea *Xenopsylla cheopis*, and other fleas, such as *Ctenocephalus canis* (Fig. 78), which is known to bite dog, man, and rat indifferently. This important conclusion is completely supported by the elaborate epidemiological observations of Thompson in Sydney, who has shown that the rat-flea theory best explains the behaviour of epidemic plague—at all events in that city.

Fig. 76.—Citellus beechyi, ground-squirrel of California. Nat. size.

Digitized by Google

Martin and Bacot's observations on plague-infected fleas are of great interest. They found that a proportion of the fleas fed on plague-infected rats develop a peculiar condition of stomach and œsophagus, these organs becoming blocked with blood-clot

Fig. 77.—Xenopsylla cheopis.

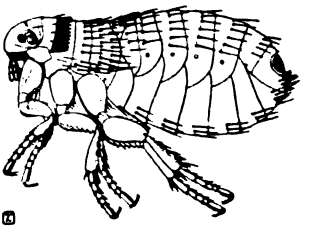


Fig. 78.—Ctenocephalus canis (female).

containing a pure culture of *B. pestis*. When such a flea feeds on a normal rat, part of the culture regurgitates and communicates infection; at the same time bacilli are passed in the fæces and

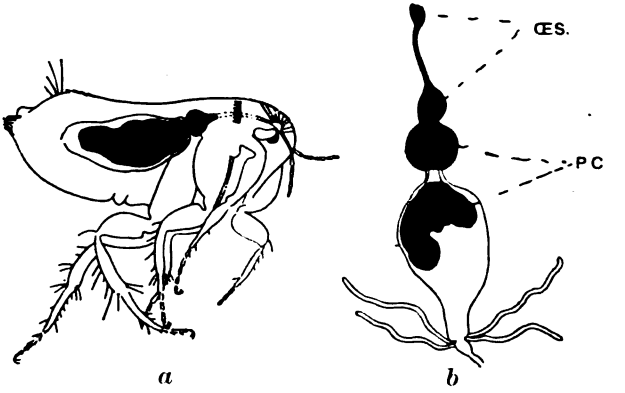


Fig. 79.—*a*, Flea viewed as a transparent object; the proventriculus and stomach contain a mass of plague-culture. *b*, Flea's stomach, obstructed by growth of plague-culture.

ŒS., Distended œsophagus containing fresh blood; P.C., obstructing mass of plague-culture.

may infect through any existing abrasion. They further observed that the "blocked" fleas died very rapidly if placed in a warm, dry atmosphere, apparently of thirst. (Figs. 79, 80.)

In temperate climates fleas are most numerous during the

Digitized by Google

warmer seasons of the year; hence summer and autumn is the bubonic plague season in such climates. In warm climates bubonic plague is most prone to become epidemic at those times of the year when temperature ranges between 10° and 30° C.—temperatures favourable to the multiplication and activity of the flea. Temperatures over 30° C. are unfavourable to the flea, especially if the atmosphere is dry. Pneumonic plague, not being spread by the flea, is not influenced by temperature in this way.

The flea, then, communicates plague either by its fouled mandibles, by regurgitation in the act of sucking, or by provoking

Fig. 80.—Edge of mass of plague-culture from flea's stomach.
Microphotograph × 1,000.

Figs. 79 and 80 illustrate the method of transmission of *B. pestis* by *Ceratophyllus fasciatus*.
(*By kind permission of Dr. C. J. Martin, "Journ. of Hyg.," 3rd Plague Suppl., Jan., 1914.*)

scratching and consequent inoculation of the bacilli deposited in its fæces.

Bionomics of the rat-flea.—In ordinary circumstances the rat-flea completes its developmental cycle in fourteen days to three weeks, but in warm, damp weather this may be shortened to ten days. The average life of a flea, apart from its host, is about ten days, but it is capable of remaining alive without food for two months, should the temperature of the air be low at the time. In tropical temperatures the insect can harbour the plague bacillus without feeding on blood for forty-five days.

Apart from the very serious danger arising from vermin affected with chronic plague, which may hang about a house for a long time, it would appear that the house itself does not retain the infection for

Digitized by Google

any length of time. The Plague Commission has shown that floors of cow-dung if contaminated with *Bacillus pestis* do not remain infective for more than forty-eight hours, and that floors of chunam cease to be infective in twenty-four hours.

Conditions favouring naturally acquired plague—The most potent circumstances which predispose to the epidemic out break of plague are extreme filth and overcrowding. In such circumstances the virus, once introduced, tends to spread. With alteration in the habits or circumstances of the population, the disease, after having become epidemic, may die out spontaneously. It may be difficult to indicate the exact way or ways in which filth and overcrowding operate; but certain it is, as experience has shown, that in good sanitary conditions plague does not spread even if introduced, and that in opposite conditions it may for a time spread like wildfire.

Except in the case of the relatively rare pneumonic form, plague, though "catching," is not nearly so contagious as are scarlet fever, measles, and smallpox.

The fact that it can be communicated to the lower animals, by feeding them on the tissues of plague patients and on cultures of the specific bacillus, suggests that it may be conveyed to man in food or drink. The bacillus is sometimes found in the intestinal contents of patients. It is also to be found in the urine. Water or food contaminated with sewage or fæcal matter may therefore be regarded as a possible medium of infection. Food contaminated by infected rats is likely also to be a source of danger.

The bacilli do not, as a rule, penetrate the unbroken epidermis, as proved by the impunity with which post-mortem examinations in plague cases have often been made; but it seems not improbable that in a proportion of instances the plague germ is introduced through trifling wounds of the feet. It is conceivable that such germs as may be lying about on the ground, deposited there in the discharges of sick human beings or of plague-stricken animals, or perhaps growing there in natural culture, may be picked up in this way. The frequency with which the primary bubo, as will be pointed out, is located in the deep femoral glands favours this idea. One can understand how insects other than fleas may act as carriers of the virus from person to person, inserting it with their bites, or inducing scratching and superficial skin lesions through which the virus obtains entrance. Yersin found that the flies in his Hong Kong plague laboratory died in great numbers, their bodies being crowded with the specific bacillus.

That the bacillus does at times enter the body through the

Digitized by Google

unbroken skin or mucous membrane is made highly probable by the certainty with which rats can be infected under experimental conditions by simply smearing a plague culture on the shaven skin.

Age, *sex*, and *occupation* have very little influence in plague. The youngest children are susceptible; old age seems to be to a certain extent protective, the disease being rarer after 50 than during adolescence. Women, doubtless on account of their remaining much indoors in tainted surroundings, are relatively more frequently attacked than men.

Atmospheric temperatures if very high or very low seem to have a repressing effect. On the other hand, plague on more than one occasion has flourished during a Russian winter. On the whole, the evidence points to moderate temperatures—50° to 80° F.—combined with a certain degree of dampness as being the principal atmospheric condition favouring epidemic outbreaks and recurrences.

In large towns and in some districts in which plague recurs for several years in succession there is a seasonal periodicity (which may not be the same in all places) of maximum and minimum prevalence.

The *duration of epidemics of plague* is very variable. In large cities—Bombay, Hong Kong, Canton, for example—when fairly established the disease may not relax its grip for ten or more years. In smaller towns it may disappear in a few months.

The *extension of plague epidemics* is peculiar; it follows trade routes. Sometimes it may spread rapidly from point to point; more generally it creeps slowly from one village to another, from one street or one house to another. Sometimes it skips a house, a village, or a district.

These and many other facts in the epidemiology of plague are probably to be explained by the connection of the disease with the rat and its flea, and depend upon the migrations of the former and the breeding seasons of the latter.

Symptoms. *Incubation period.*—Symptoms of plague begin to show themselves after an incubation period of from two to eight, rarely fifteen days.

The average case of plague: Prodromal stage.—In a certain but small proportion of cases there is a prodromal stage characterized by physical and mental depression, anorexia, aching of the limbs, feelings of chilliness, giddiness, palpitations, and sometimes dull pains in the groin at the seat of the future bubo.

Digitized by Google

Stage of invasion.—Usually, the disease sets in somewhat suddenly with fever, extreme lassitude, frontal or, more rarely, occipital headache, aching of the limbs, vertigo, drowsiness or perhaps wakefulness, or troubled dreams. Rigor is rarely a marked feature; more often the disease is heralded by feelings of chilliness. The face quickly acquires a peculiar expression, the features being drawn and haggard, the eyes bloodshot, sunken and staring, the pupils probably dilated; sometimes the face wears an expression of fear or horror. The patient, when he can walk, drags himself about in a dreamy sort of way, or he staggers like a drunken man. There may be nausea and vomiting; in some instances there is diarrhœa.

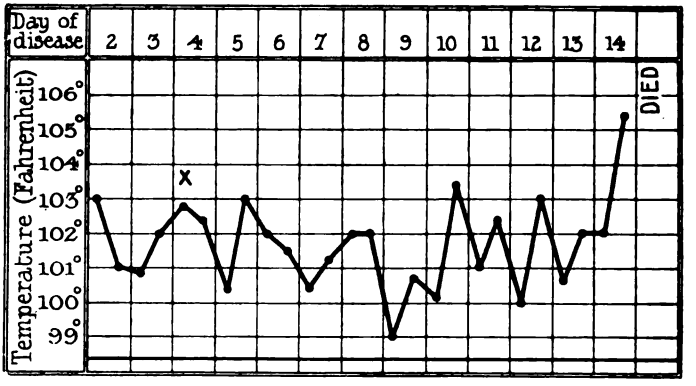


Chart 13.—Plague. (*Bellingham-Smith.*)
× *B. pestis* isolated from the blood.

Stage of fever.—The stage of invasion may last for a day or two without a serious rise of temperature occurring. Usually it is of much shorter duration; or it may be altogether wanting, the disease developing abruptly without definite rigor or other warning, the thermometer rising rapidly to 103° or 104° (Chart 13), or even to 107° F., with a corresponding acceleration of pulse and respiration. The skin is now dry and burning, the face is bloated, the eyes are still more injected, sunken and fixed, the hearing is dulled. The tongue is swollen and covered with a creamy fur, which rapidly dries and becomes brown or almost black; sordes form on the teeth and about the lips and nostrils. Thirst is intense, prostration extreme, the patient from utter weakness being hardly able to make himself heard. Sometimes he becomes delirious: the delirium may be wildly furious, or fatuous, or of a low muttering type. Coma,

Digitized by Google

convulsions—sometimes of a tetanic character—retention of urine, subsultus tendinum, and other nervous phenomena may occur. Vomiting is in certain cases very frequent; some are constipated, others have diarrhœa. The spleen and liver are usually both enlarged. Urine is scanty, but rarely contains more than a trace of albumen. The pulse, at first full and bounding, in the majority of cases rapidly loses tone, becoming small, frequent, fluttering, dicrotic, intermittent. In the later stages the heart may be dilated, the first sound being feeble or absent.

Bubonic plague.—In about three-fourths of the cases, some time between the first few hours and the fifth day, generally within twenty-four hours, the characteristic bubo or buboes develop. Usually (in 70 per cent.) the bubo forms in the groin, most frequently on the right side, affecting one or more of the femoral glands; less frequently (20 per cent.) it is in the axillary glands; and still more rarely (10 per cent.), and most commonly in children, it is the glands at the angle of the lower jaw that are affected. The buboes are usually single; in about one-eighth of the cases, however, they form simultaneously on both sides of the body. Very rarely are buboes formed in the popliteal or in the epitrochlear elbow glands, or in those at the root of the neck. Occasionally buboes occur simultaneously in different parts of the body.

The buboes vary considerably in size. In some instances they are not so large as a walnut; in others they attain the size of a goose's egg. Pain is often very severe; on the other hand, it is sometimes hardly complained of. Besides the enlargement of the gland, there is in most instances distinct infiltration of the surrounding connective tissue.

In a very small proportion of cases what are usually described as carbuncles, but which are in reality small patches of moist gangrenous skin that may gradually involve a large area, develop on different parts of the integument. These occur either in the early stage or late in the disease. Sometimes they slough and lead to extensive gangrene.

In favourable cases, sooner or later, after or without the appearance of the bubo, the constitutional symptoms abate with the setting in of profuse perspiration. The tongue now begins to moisten, the pulse-rate and temperature to fall, and the mild delirium, if it has been present, to abate. The bubo, however, continues to enlarge and to soften. After a few days, if not incised, it bursts and discharges pus and sloughs—sometimes very ill-smelling. In rare instances suppuration is delayed for weeks; whilst in some the bubo

Digitized by Google

subsides after a few weeks, or perhaps months, without having broken down. Convalescence, when it occurs, sets in some time between the sixth and tenth day, although it may be delayed for a fortnight or three weeks. Occasionally a pyæmic condition, with boils, abscesses, cellulitis, parotitis, or secondary adenitis, succeeds the primary fever. The sores left by the buboes and abscesses of plague are extremely indolent and may take months to heal.

Hæmorrhages of different kinds are not an unusual feature of plague. Ecchymotic effusions of a purplish or dull-red tint, and varying in size from a hemp-seed to spots half an inch in diameter, are very often found scattered in greater or less profusion over the skin, especially on exposed parts of the body and at the sites of insect bites or of wounds. Larger patches of cutaneous hæmorrhagic effusion are rare. There may be bleeding from the nose, mouth, lungs, stomach, bowel, or kidneys. Hæmorrhages occur with marked frequency in certain epidemics; they are regarded as evidence of great malignity. Especially malignant are those epidemics in which hæmoptysis, or pneumonia, is a common occurrence.

Abortion almost invariably occurs in pregnant women; the fœtus sometimes shows signs of the disease.

Death may take place at any time in the course of plague. Usually it occurs between the third and fifth day, with symptoms of profound adynamia, heart failure, or perhaps from convulsions, from coma, from internal hæmorrhage, or, later, from exhaustion consequent upon prolonged fever or suppuration, or from secondary hæmorrhages.

Certain epidemics are distinguished by the large proportion of mild cases. In such, buboes form and suppurate or resolve, the associated constitutional symptoms being comparatively mild, or perhaps altogether wanting. In every epidemic there may be cases in which the patient is able to be about, having little if any fever and, apparently, being little inconvenienced by the disease. Such cases, however, may collapse suddenly.

Septicæmic plague, or pestis siderans.—In this type there is no special enlargement of the lymphatic glands apparent during life, although after death the glands throughout the body are found to be somewhat enlarged and congested. The high degree of virulence and the rapid course of the disease depend on the entry of large numbers of the bacilli into the blood, where they can be readily found during life. The patient is prostrated from the outset; he is pale and apathetic; there is generally

Digitized by Google

little febrile reaction (100° F.). Great weakness, delirium, picking of the bedclothes, stupor, and coma end in death on the first, second, or third day. Frequently in these cases there are hæmorrhages.

Pneumonic plague.—This type, which was carefully studied by Childe and others, is especially dangerous to the patients, attendants, and visitors, as well as deadly; dangerous because of the multitude of bacilli which are scattered about in the patient's expectoration,* and because the clinical symptoms are unlike those of typical plague and are apt to be mistaken for some ordinary form of lung disease. The illness commences with rigor, malaise, intense headache, vomiting, general pains, fever, and intense prostration. Cough and dyspnœa set in, accompanied by a profuse, watery, blood-tinged sputum. The sputum is not viscid and rusty, as in ordinary pneumonia. Moist râles are audible at the bases of the lungs, the breathing becomes hurried, other symptoms rapidly become worse, delirium sets in, and the patient usually dies on the fourth or fifth day. This is the most fatal as well as the most directly infectious form of plague.

Relapses, though rare, do occur, and are dangerous.

Mortality.—The case-mortality of bubonic plague varies in different epidemics. It is usually greatest at the beginning and height of the epidemic. The death-rate may be anything from 60 to 95 per cent. of those attacked. Much appears to depend on the social condition of the patient and the attention and nursing available. Thus in a recent Hong Kong epidemic, whilst the case-mortality among the indifferently fed, overcrowded, unwashed, and almost unnursed Chinese amounted to 93·4 per cent., it was only 77 per cent. among the Indians, 60 per cent. among the Japanese, and 18·2 per cent. among the Europeans—a gradation in general correspondence with the social and hygienic conditions of these different nationalities. In the South American epidemics and in the recent circumscribed epidemics in Europe the mortality was only about one-third of that obtaining in India and China. Pneumonic plague is generally fatal in from three to four days.

Morbid anatomy and pathology.—After death from plague the surface of the body very frequently presents numerous ecchymotic spots or patches. The number and extent of these vary, apparently, in different epidemics. In some epidemics the cutaneous hæmorrhages have been both extensive and numerous; hence the name "black death" formerly applied to

* During the epidemic of pneumonic plague in Manchuria in 1910-11, Strong and Teague exposed agar plates at distances varying from 5 cm. to 2 metres in front of the faces of plague patients, and a proportion yielded plague-cultures. In the epidemic there were only two or three deaths from bubonic plague out of a total of 50,000 cases.

Digitized by Google

this disease. The characteristic buboes are generally apparent; occasionally there are also furuncles, pustules, and abscesses. Rigor mortis is usually moderate; sometimes post-mortem muscular contractions, like those in cholera, take place. Post-mortem rise of temperature is often observed. Decomposition is said to set in early.

The characteristic appearance in a necropsy of plague is that of engorgement and hæmorrhage, nearly every organ of the body participating more or less. There is also parenchymatous degeneration in most of the organs. The brain, spinal cord, and their meninges are markedly congested, and there may be an increase of subarachnoid and ventricular fluid. There are numerous and pronounced puncta cruenta on the brain sections; occasionally there may be considerable extravasations of blood into the substance of the brain (mesocephalon and medulla oblongata).

Ecchymoses are common in all serous surfaces; the contents of the different serous cavities may be sanguineous. Extensive hæmorrhages are occasionally found in the peritoneum, mediastinum, trachea, bowel, stomach, pelvis of kidney, ureter, bladder, or in the pleural cavities. The lung frequently shows evidences of bronchitis and hypostatic pneumonia; sometimes hæmorrhagic infarcts and abscesses are found. The right side of the heart and the great veins are usually distended with feebly coagulated or fluid blood. In pneumonic plague the superficial lymphatic glands are not enlarged; the pleural cavities contain blood-stained serum; the infected lungs are deeply congested and œdematous, and at a later stage pneumonic consolidation is found. The bronchi contain blood-stained serum and the bronchial glands are swollen and hæmorrhagic.

The liver is congested and swollen and its cells are degenerated. The spleen is enlarged to two or three times its normal size. The kidneys are in a similar condition. The mucosa of the alimentary canal as a whole is congested, showing here and there punctate ecchymotic effusions and, occasionally, hæmorrhagic erosions, and even—especially about the ileo-cæcal valve—ulcerations.

Evidence is invariably discoverable of serious implication of the lymphatic system; around the glands there is much exudation and hæmorrhagic effusion, with hyperplasia of the gland cells, and an enormous multiplication of bacteria.

Diagnosis.—The occurrence of fever and adenitis during a plague epidemic must invariably be viewed with suspicion, and particularly if the fever rapidly assumes an adynamic character. In the early stages diagnosis may be very doubtful, especially in pneumonic plague, and in the countries of high filarial endemicity and in which filarial adenitis is necessarily a common occurrence. The discovery of the bacillus in the glands, blood, sputum, or discharges is the only thoroughly reliable test. Should a cocco-bacillus be found with the characteristic bipolar staining, it should be cultivated by Haffkine's method in broth on which clarified butter (ghee) or coco-nut oil is floated. (*See* p. 255.) In case of doubt, animal inoculation should be had recourse to: a little of the virus from the patient or a culture is rubbed into a shaven area (1 in. square) on the abdomen of a white rat or a guinea-pig. *B. pestis*

Digitized by Google

inoculated in this way kills the guinea-pig in seven days, the rat sooner.*

General prophylaxis.—The prophylaxis of plague, as of other infectious diseases, has to be considered from the standpoint of the community and also from that of the individual. As regards the former, it includes measures for preventing the introduction of the virus, for staying its spread if introduced, and for securing its destruction.

Quarantine.—Modern systems of land or sea quarantine directed against plague take cognizance of the facts that the incubation period of the disease may extend to ten days, and that plague affects certain of the lower animals as well as man. Ten days is the minimum period that should elapse between the time of departure from an infected place, between the date of the last death, or between the arrival of a ship or batch of travellers with cases of plague in progress among them, and the granting of free pratique. Moreover, as Kitasato has shown that the specific bacillus persists in the bodies of those who have recovered from plague for at least three weeks from the cessation of the active disease, convalescents should be isolated for a month before they are allowed to mingle with an uninfected community.

Although Kitasato has stated that the plague bacillus perishes in four days when dried on cover-glasses and protected from sunlight, and in from three to four hours when exposed to sunlight, experience has shown that under certain conditions, as yet unknown, it will survive outside the body for a very much longer period, apparently a year or more.† There is a considerable mass of evidence tending to show that clothes, skins, textile fabrics, and similar materials may preserve the virus in an active state for several months.

In ships coming from an infected port the rats, mice, and such-

* *Post-mortem indications of plague in the rat.*—Before rats suspected of being plague-infected are handled, they should be immersed in disinfectant to destroy ectoparasites.

The lymphatic glands should be first exposed. If the rat is infected, subcutaneous injection around the glands is generally recognizable. If the gland is itself inflamed it is almost diagnostic of plague; in which case the liver will be found of a yellow colour and sprinkled with innumerable pinky-white granules. The spleen is enlarged, congested, and occasionally granular. Serous or blood-stained serous effusions are present in 72 per cent. of such rats. If on microscopical examination of scrapings from glands or spleen bipolar-staining bacilli are detected the case is probably plague. Too great stress must not be laid on bipolar staining alone, as this feature depends somewhat on the method of staining; it is best demonstrated by Leishman eosin-azur stain or Archibald's stain. (For the composition of Archibald's stain *see* Appendix III., p. 929.)

† Schurupoff found seven-year-old cultures of *B. pestis* to be still alive. He examined 17 plague corpses a year after death; from 6 of them he recovered the plague bacillus.

Digitized by Google

like vermin should be destroyed, thrown overboard and sunk before harbour is entered. The generation of sulphurous acid gas under pressure, especially by the Clayton system, has been found useful for this purpose.

The most suitable and practicable disinfectants are steam, 1 : 1,000 corrosive sublimate in carbol-sulphuric acid, lysol, chloride of lime in 1-per-cent. solution, carbolic acid in 5-per-cent., and formalin 2-per-cent.

On plague breaking out in a small village community, so soon as the disease is recognized measures should be taken to prevent the inhabitants leaving the locality and thus spreading the disease. There is little danger of this until the inhabitants become alarmed by a rapid extension of the disease. If possible, after the patients have been isolated in a special hospital, the village should be evacuated for a month, the inhabitants being accommodated in temporary huts close by, while the houses which the patients have occupied and those in their neighbourhood should be disinfected. The safest and most thorough form of disinfection is by fire, and in the case of an isolated village prompt destruction of the infected houses by fire is the surest method of stamping out the infection. The clothes and bedding of all patients should be burned. The dead, with as little delay as possible, should be buried in deep graves or cremated. Isolated observation camps should be organized, in which " suspects " and " contacts " may be segregated for a time equal at least to the incubation period of the disease. War should be waged against all rats and mice, and their corpses burned.

In the event of an outbreak in a town, it must be borne in mind that plague, once established in human beings, is communicable to others and to rats by means of the expectoration, by the discharges from the bowels and by the urine, and by discharges from the buboes or glandular swellings ; and that a plague in rats usually precedes plague in human beings. In addition, therefore, to prompt notification of plague patients, a system designed to obtain information as to the occurrence of plague in rats should be instituted. Every rat destroyed must be bacteriologically examined.

For the detection of plague-infected houses, guinea-pigs, which do not harbour fleas as a rule, are now employed in Japan and India as convenient traps for rat-fleas. The guinea-pigs are turned loose in houses and warehouses, and rapidly succumb to the disease if plague fleas are present.

In India the compulsory inspection of all dead bodies prior to

Digitized by Google

burial has been found a valuable measure for discovering infected houses and localities.

It is very questionable if, in practice, any system of rigid quarantine, no matter how carefully devised and theoretically perfect, is ever absolutely protective. Even if the introduction of plague by man could be prevented in this way, it is difficult to see how its introduction by rats or mice could be effectually guarded against. Quarantine must be combined with careful general sanitation, with thorough disinfection, with the destruction of all discharges and fomites, with the speedy discovery and isolation of the sick, with the evacuation of infected houses and even of neighbourhoods, and with the wholesale destruction of vermin. These latter things English experience has shown to be far more effective than any system of quarantine; it was only in deference to Continental views that quarantine, in the ancient sense of the word, was practised in Great Britain against plague and yellow fever. A rational, practicable quarantine plus rational sanitary measures is what is wanted.

Destruction of vermin and other measures in anticipation of the introduction of plague virus.—The campaign against rats is usually carried on by the employment of rat-traps and rat-catchers, and the cautious laying down of poisons such as arsenic, phosphorus, and baryta. As no one method is satisfactory, it is usual to employ several at the same time. The pumping of SO_2 gas under pressure is useful for ships full of cargo and for warehouses with goods in them. So long as the sulphurous acid gas is dry, and is not used on damp articles, no damage is done to merchandise. Care has, however, to be taken with damp things, as they may get slightly discoloured.

Where possible, houses and warehouses should be made rat-proof —not an easy measure, considering the burrowing and climbing habits of the rat. *Rattus norvegicus* can penetrate ordinary lime-mortar or soft brick, but is stopped by cement and concrete. Its burrows may attain a depth of 18 in. *Rattus rattus* is not so active in this respect. Simpson recommends that walls should be at least 6 in. thick when made of hard brick or concrete, and that they should extend to not less than 18 in. below the level of the ground floor, and the latter should be paved with concrete 3 in. thick, covered with $\frac{1}{2}$ in. of cement. All ventilators should be protected with iron gratings, and all openings around wires and pipes cemented. The mooring cables of ships should be shielded in such a way as to prevent egress or ingress of rats, and all gangways should be taken up at night or when not in use.

Digitized by Google

Attempts have been made to set up an epidemic disease, other than plague, among the rats, which should not be communicable to man. For this purpose the bacillus discovered by Danysz was recommended by him. But the method employed—viz. inoculating a few rats with the bacillus and then allowing them to escape, in the hope that when they sickened they would be eaten by other rats, which would in their turn be taken ill, and an epidemic be thus set up—has not been successful. Experiments on these lines have failed. The bacillus was, however, found to be useful in Cape Town and elsewhere for the destruction of rats when a system introduced by Professor Simpson was adopted, and bread soaked in the cultures was distributed and laid down in the same way as is usually done with biscuits on which rat poison is spread. By distributing thousands of doses an excellent result was obtained, and rats which were examined in the localities where the Danysz bacillus had been used in this way were found to have died from the disease induced by this organism. The virulence of the cultures can be maintained by growing them on egg-albumen and frequent *passage* through experimental rats.

Personal prophylaxis.—As regards the individual, all unnecessary visits either to plague patients or to plague neighbourhoods should be avoided and, if possible, prevented. The attendants on the sick ought especially to take care that the ventilation of the sick-room is thorough, that cubic space is abundant, and that the utmost cleanliness is practised. Nurses must not hang over patients unnecessarily; they must also be careful to seal up and cover any wounds, no matter how trifling, they may have on their hands. Stools and urine must be disinfected, and hands frequently washed. To obviate risk from wounds and to prevent the access of fleas and similar suctorial insects, those engaged on plague duties should wear boots and have the legs protected by trousers tied tightly round the ankles or, better, by putties. Leather gloves are advisable if there is much handling of furniture or of anything likely to abrade the skin. *Cats or dogs should not be allowed near plague patients.*

The attendants on pneumonic cases should provide themselves with masks of muslin, three or four fold, and changed when at all damp, and also with goggles to protect the eyes. In Mukden a mask of absorbent cotton-wool (16 by 12 cm.) enclosed in muslin, and retained in position by a many-tailed gauze bandage, together with goggles, rubber gloves, and cotton uniform, proved thoroughly effective.

Haffkine's inoculations. — Early during the Bombay epidemic

Digitized by Google

Haffkine introduced a system of prophylactic inoculation which is of proved value, both in reducing the number attacked with plague to the extent of from 77 to 85 per cent., and in diminishing by 80 per cent. the mortality in those attacked. It consists essentially in the subcutaneous injection of six-weeks-old cultures of plague bacilli incubated at 25°–30° C. and killed by heat—65° C. for one hour; carbolic acid, 0·5 per cent., is then added: up to 4 c.c. are injected according to the size and age of the individual. The Indian Plague Commission reports strongly in favour of these inoculations. All plague laboratory workers and all who are likely to be exposed to plague infection should receive them. The protection they confer lasts about twenty months. In the Report of the Bombay Bacteriological Laboratory, 1911, Glen Liston states that in the inoculated the incidence of plague was 8 per 1,000 of the population concerned, whereas it was 34 per 1,000 in the uninoculated in the same communities; the case-mortality in the inoculated was 39·5 per 1,000 attacked, in the uninoculated 78 per 1,000. The best results are obtained from a two-months growth which has been stored about eighteen months. The prophylactic needs great care in its preparation. Its storage in hermetically sealed bottles should be insisted upon, and every bottle ought to be tested before use. The resulting reaction is sometimes severe. Pratt-Johnston has advocated a prophylactic made from young agar cultures in 1 c.c. ampoules, as producing a less severe and yet equally efficacious reaction.

Lustig's injections.—Lustig and Galeotti introduced a method of preventive inoculation which, they say, obviates many of the drawbacks of Haffkine's. They dissolve agar-agar plate cultures of *Bacillus pestis* in 1-per-cent. solution of caustic potash, precipitate the nucleo-proteins so dissolved by weak acetic or hydrochloric acid, collect the precipitate, wash and dry it *in vacuo*. This substance, apparently, can be kept for an indefinite time. The dose for a man is about 3 mg. Before it is injected subcutaneously it is dissolved in a convenient quantity of 0·5-per-cent. solution of carbonate of soda. Its injection is followed by marked local and general reaction, and in the case of the lower animals by at least temporary immunity from plague. Favourable results have been obtained in man.

So far, Haffkine's prophylactic is the one most frequently used and gives the best results.

Treatment.—The treatment of plague is mainly symptomatic. In attempting to relieve symptoms the asthenic tendencies of the disease must ever be borne in mind, and depressant remedies of all kinds carefully avoided.

During the earlier stages, when headache and perhaps high fever are urgent, much relief may be obtained from ice-bags to the

Digitized by Google

head and neck. If it be deemed advisable to attempt to lower the temperature, sponging of the body every hour with warm water is a much safer measure than the employment of such antipyretics as antipyrin and similar drugs. Vomiting is usually relieved by a full dose of calomel followed by a saline. If this does not succeed, or if diarrhœa be present, Lowson recommends ice pills and an effervescing mixture containing morphia and hydrocyanic acid. Sinapisms to the epigastrium are useful. In collapse, stimulants of various kinds, including strong ammonia to the nostrils and ether hypodermically, are indicated; they sometimes succeed in resuscitating a sinking patient. Given with judgment, morphia is by far the best hypnotic. Hyoscine ($\frac{1}{200}$ to $\frac{1}{75}$ gr.) or chloral (20 gr.) and bromide of potassium (30 gr.) are of service for the same purpose. Diarrhœa, if urgent, is best treated by intestinal antiseptics, as salol in 10-gr. doses every four hours. The buboes in the early stage may be treated with applications of glycerin and belladonna. Should they become red and inflamed they must be poulticed and, on softening occurring, incised and dressed with iodoform. Indolent bubonic swellings should be treated with iodine liniment. Feeding and stimulation are to be conducted on ordinary principles.

Serum-therapy.—Yersin, Calmette, and Borrel found they were able to immunize rabbits by intraperitoneal and subcutaneous injections of gelatin cultures of plague heated for one hour to 58° C. Subsequently they immunized a horse by intravenous injections of living virulent cultures and produced an effective antiserum. It must be given intravenously in large doses (100–250 c.c.), and frequently repeated. Unfortunately in practice this serum has proved disappointing, at the best but modifying the course of the disease and prolonging life.

Connor and others have reported favourable results from intravenous injections of iodine (iodine 1 part, distilled water 60 parts) and eusol, frequently administered.

Description of the Commoner Species of Rat concerned in the Spread of Plague

An intimate knowledge of the appearances and habits of the many species of rats is hardly necessary to the tropical specialist; considering the important rôle several species play in the spread of plague he should, however, be in a position to identify the more domestic varieties. For this purpose the subjoined Table, contributed by Mr. M. A. C. Hinton, will be found of considerable assistance.

Digitized by Google

Rattus rattus, Linn. — Build slender; muzzle sharp; ears large, translucent; tail usually much longer, never much shorter than head and body; hind foot (heel to tip of longest toe, without claw) 35–40 mm.; weight of adults rarely more than 8 oz. Indigenous, wild, more or less arboreal in Indo-Burmese countries. The chief domestic races are distinguished as follows:—

A. Back reddish or greyish-brown.
  a. Under parts pure white or pale lemon. *R. r. frugivorus*, Raf. (= *tectorum*). Common in Mediterranean region.
  b. Under parts darkened.
    a^1. Ventral hairs with rusty tips. *R. r. rufescens*, Gray. Common rat of Indian houses.
    b^1. Ventral hairs without rusty tips. *R. r. alexandrinus*, Geoff.
B. Back black; under parts dusky or slate-grey. *R. r. rattus*, Linn. Essentially a domestic form which has been evolved in cold temperate countries.

The forms *frugivorus*, *alexandrinus*, and *rattus* have now acquired an almost worldwide distribution; *frugivorus* is the least, *rattus* the most modified race. These are climbing rats, common on ships; frequent in dwellings in warm countries, and not shunning man; they are of especial importance as plague-carriers; attain sexual maturity early (min. weight sex-mature = 70 grm.); breed throughout the year; gestation about 21 days, but with concurrent lactation about 31 days; litter of from 4 to 11; average litter 5 or 6.

Rattus norvegicus, Berkenhout (= **decumanus**).—Robust; muzzle blunt; ears small, opaque; tail noticeably shorter than head and body; hind foot 40 to 45 mm.; weight of adults commonly 17 oz., often much more; colour brown or grey above, silvery below: a melanic form (often confused with *R. rattus*) quite common.

Indigenous to Central Asia; now common in all temperate countries. Infests drains and waterways; common in cellars and basements, but shunning mankind as a rule. Breeding and gestation as in *R. rattus* (min. weight sex-mature = 100 grm.); litter of from 6 to 23; average litter 8 to 10.

Fleas

Readers in search of information upon the natural history and classification of these insects are referred to p. 869, where the subject is sufficiently dealt with for the purposes of the tropical practitioner.

Digitized by Google

CHAPTER XX

UNDULANT FEVER

Synonyms. — Febris Undulans; Malta Fever; Mediterranean Fever.

Definition.—A disease of low mortality, indefinite duration, and irregular course, undulant fever is the result of infection by a specific germ—*Micrococcus melitensis.* In its more typical form it is characterized by a series of febrile attacks, each individual attack, after lasting one or more weeks, gradually subsiding into a period of absolute or relative apyrexia, also of uncertain duration. Common and characteristic complications are rheumatic-like affection of joints, profuse diaphoresis, anæmia, liability to orchitis and neuralgia.

Geographical distribution.—Undulant fever was somewhat unfortunately named Malta fever, for we now know that the disease which was so designated is not, as was formerly supposed, confined to Malta, or even to the Mediterranean. It is very common there, particularly in Malta and the eastern and southern littoral of the Mediterranean; but recent investigations show that it occurs in Italy, France, Spain, the Red Sea littoral, India, China, South Africa, Somaliland, West Africa, the West Indies, the Brazils, the United States, and even in England. Manson saw two cases that originated in England, which gave typical serum reactions. It is highly probable, therefore, that the same, or a similar, fever occurs in many other parts of the world, having been confounded hitherto with malarial fever or with typhoid. This conviction is based on clinical rather than on laboratory observation.

As it is extremely prevalent at times in the Mediterranean fleet and in the garrisons of Gibraltar and Malta, this disease is specially interesting to naval and military surgeons. Although only occasionally proving fatal, it is a fruitful source of inefficiency and invaliding.

Until comparatively recently it appeared to be on the increase in its old haunts, and to be becoming common in places where it was formerly rare—Port Said and Egypt, for example.

The following figures, supplied by Bassett-Smith, show its im-

Digitized by Google

portance formerly to our Naval and Military Services in the Mediterranean :—

INCIDENCE OF UNDULANT FEVER

	Army			Navy			Total days' sickness
	Strength	Cases	Deaths	Strength	Cases	Deaths	
1900	9,203	171	10	14,250	356	6	22,998
1901	9,384	288	10	14,070	286	3	16,987
1902	10,889	198	10	18,470	436	3	27,432
1903	10,608	507	11	18,410	400	6	30,541
1904	10,615	429	15	19,590	430	9	28,458

History.—Formerly undulant fever was confounded with typhoid and malaria. The labours of clinical observers from Marston (1861) to Maclean (1885), and more especially the bacteriological researches of Bruce (1887), Hughes, Gipps, Wright, Semple, and Bassett-Smith, have established it as a special disease. More recently an important advance of great practical value has been made by a Royal Society Commission, which has shown that the germ of this fever infects several of the lower animals, especially goats, in whose milk and urine it is excreted.

Etiology.—Bruce, in 1887, demonstrated the presence in the spleen in undulant fever of a special bacterium—the *Micrococcus melitensis*—and by a series of experiments proved that it was the cause of the disease. Unfortunately, as the bacterium occurs only sparsely in the general circulation (unless in the earlier stages, when the temperature is high), to search for it in the blood in the later stages of the disease does not aid in diagnosis ; but pathologically Bruce's discovery is of great importance, as it enables us to say positively that undulant fever is a distinct disease, altogether different from either typhoid or malaria. The organism is present in abundance in the spleen pulp, and also in the lymphatic glands, in which it persists longer than elsewhere, and from both of which it can be recovered by cultivation. Bruce found it in the spleen in ten fatal cases. His results have been confirmed by Hughes, Gipps, Wright, Durham, Bassett-Smith, and many others. Injections of pure cultures give rise to a similar disease in monkeys and other animals, from whose blood the micrococcus can be recovered, cultivated afresh, and, on injection into other animals, again give rise to the disease. In five recorded instances inoculation—intentional and accidental—of cultures of the micrococcus into man has been followed by the characteristic symptoms of undulant fever after an incubation period of from five to fifteen days.

In recent years a variety of the micrococcus (*M. paramelitensis*), which gives different serological reactions from those of the original

Digitized by Google

strain, has been recognized as being responsible for those cases of clinical undulant fever which do not give the Widal reaction with cultures of *melitensis*.

The *Micrococcus melitensis* measures 0·33 μ in diameter. It occurs generally singly, often in pairs, sometimes in fours, but never, unless in culture, in longer chains. According to Gordon, it possesses one to four flagella. It is Gram-negative and readily stained by a watery solution of gentian violet, and is best cultivated in a 1½-per-cent. very feebly alkaline peptonized beef agar; in this medium, some time after inoculation, it appears as minute, clear, pearly specks. After thirty-six hours the cultures become a transparent amber; later they are opaque. No liquefaction occurs in gelatin. The individual colonies are small, round, somewhat raised discs growing to 2–3 mm. in diameter about the ninth day. The optimum temperature for growth is 37° C. In bouillon it produces a general turbidity.

At one time believed to be a delicate organism, recent investigations have shown that the micrococcus can live for a long time in water, in dust, or on the clothes of patients, and that it is not killed by cold or desiccation. Moreover, it is now known that it is excreted in the urine of man in 10 per cent. of convalescent cases, and that it occurs in great abundance in the milk and urine of apparently healthy Maltese goats (50 per cent.), cows, and in the urine of apparently healthy men. It is also found in dogs (9 per cent.), sheep, and horses. These facts account in part for the great frequency and dissemination of the disease in such insanitary places as Malta, to which place they specially refer.

M. melitensis can be cultured from the bloodstream during the height of the fever in a considerable proportion of cases; for this purpose 5–10 c.c. of blood should be withdrawn from a vein and well diluted in flasks, each containing 50 c.c. of bouillon. It has occasionally been obtained from the fæces. The serum of undulant fever cases, as well as the milk of infected goats, will agglutinate it.

Influence of age and residence.—The most susceptible age is between the sixth and the thirtieth year. Length of residence does not influence susceptibility. In Malta the natives suffer as well as visitors.

Influence of season.—In Malta and other places where the disease is endemic this fever occasionally assumes an epidemic character. The period of its greatest prevalence in Malta is the season of lowest rainfall, embracing June, July, August, and September; differing in this respect from typhoid, which, in that island, is more prevalent during the succeeding months. It is not

Digitized by Google

confined absolutely to the summer months; cases occur all the year round.

Local causes.—The disease tends to occur in particular towns or villages, in particular houses, barracks, hospitals, and rooms and in particular ships, manifestly originating in limited foci of infection. At one time the weight of evidence was regarded by some as pointing to its diffusion by air currents, and not by food or water. There is no absolute certainty on these points. Evidence is rapidly accumulating to show that milk is the most important medium.

Formerly it was supposed that in Malta this fever was linked to the immediate neighbourhood of the seashore, and tha the sewage-laden, tideless condition of the harbour at Valetta was somehow responsible for its prevalence there. Zammit has shown, however, that the disease occurs all over the island, and that in some instances it is more prevalent in certain inland and relatively sanitary villages than in more insanitary towns and villages on the coast. Certain ships are notoriously foci of the disease, and are believed to carry the infection. Manson saw a medical man suffering from a chronic fever, whose blood, in expert hands, gave the characteristic reaction, and who, if he had undulant fever, certainly got it from a ship which had recently been to the Mediterranean. The patient had never been in that part of the world, and had not been out of England for a year.

Influence of social conditions.—All classes are liable to this disease; the officer and his family as well as the soldier in barracks or the sailor on shipboard. The organism has been found in the mother's milk, so may presumably be transmitted to sucklings.

Mode of infection.—Although the possibility must not be ignored, undulant fever is not generally transmitted directly from one person to another; that is to say, is not usually directly communicable from the sick to the healthy. The germ is readily conveyed by inoculation; the prick of a contaminated needle will suffice. Moreover, it is a well-recognized fact that, of all infections, undulant fever is the most easily acquired in the laboratory from the handling of cultures. Living emulsions of *M. melitensis* should never be handed round for class work. Zammit and others seek to incriminate the mosquito as an inoculator, and point, in support of their contention, to the special prevalence of the disease in the mosquito season, to the facts that of 896 mosquitoes examined bacteriologically the germ was found in 4, and that the disease has twice been conveyed to monkeys by infected insects.

Digitized by Google

A very striking circumstance is that in some hospitals the nurses and attendants in the fever wards are ten times more liable to contract the disease than people not so employed.

Possibly the infection is blown about by winds as dust, and being inhaled, or falling into the conjunctival sac, or on a wound or sore, obtains an entrance. Bearing in mind the presence of the germ in the excreta of man and animals, the dusty character of the soil of Malta and many Mediterranean towns, the extremely minute dose of a culture required for a successful inoculation, in any or all of these ways infection seems possible. Manson recorded a case, originating in England, in which a father was apparently infected by placing in his mouth the clinical thermometer used by his son recently invalided from Malta on account of the disease.

It is now known that the infection is most usually conveyed in milk, and it has been suggested that it may be introduced in other kinds of food, or in water. Water as a usual medium may be dismissed, but there is strong evidence, judging from naval and military opinion, that, though the usual, milk is not the only medium. Facts point very distinctly to goat's milk as the most important medium of infection. The micrococcus is present in the milk of 10 per cent. of Maltese goats. Monkeys are easily infected by feeding them on such milk. Immediately on the goat's milk supply to the naval and military hospitals in Malta being stopped the cases of locally acquired undulant fever practically ceased. Formerly this fever was very common in Gibraltar. The milk supply of the garrison at that time was largely from goats imported from Malta. Gradually these goats have died out or been got rid of, and no more Maltese goats have been imported. Concurrently with this there has been a marked and proportional reduction of undulant fever cases in the garrison. There is one well-authenticated instance of wholesale infection from this source in the case of the s.s. *Joshua Nicholson*, which shipped 65 goats in Malta ; an epidemic of undulant fever broke out on board, and nearly all those who drank the milk of the goats were attacked.

Immunity.—Bruce holds that one attack confers immunity from subsequent attacks ; other authorities believe that one attack, so far from conferring immunity, actually predisposes to subsequent attack. The latter is Bassett-Smith's opinion, based on the fact that he finds the bactericidal power of the serum and the phagocytic energy of the leucocytes lowered during, and for some considerable time after, an attack of the disease.

Incubation period.—The period of incubation in the naturally acquired disease is difficult to fix. Cases have occurred as early as

Digitized by Google

six days after arrival in Malta ; others as late as fourteen and seventeen days after the subject of it has quitted Malta. Some have held that it may remain latent for months.

Symptoms.—Undulant fever begins generally with lassitude and malaise, such as we associate with the incubation of many specific fevers, particularly typhoid. There are headache, boneache, anorexia, and so forth. At first the patient may go about his work as usual. Gradually the daily task becomes increasingly irksome, and he takes to bed. Headache may now become intense, and, in addition, the patient will suffer from thirst and constipation. At the commencement the symptoms, except that there is very rarely diarrhœa, resemble those of typhoid. There are no rose spots, however, then or at any subsequent period. There is evidence in the coated tongue, which looks as if covered with white paint, in the congested pharynx, the anorexia, and the epigastric tenderness, of gastric catarrh ; and the occasional cough and harsh, unsatisfactory breathing at the bases of the lungs indicate some degree of bronchitis or of pulmonary congestion. There may also be delirium at night. The fever is usually of a remittent type, the thermometer rising towards evening and falling during the night, the patient becoming bathed in a profuse perspiration towards morning. The spleen and the liver, but especially the former, are somewhat enlarged and, perhaps, tender. Lumbar pain may be urgent.

After a week or two of this type of fever, specially distinguished by pains and perspirations, the tongue begins to clean and the appetite to revive ; but, notwithstanding these signs of amendment, the patient still remains listless and liable to headache and constipation. He continues feverish and at times perspires profusely. Gradually, however, although the patient is anæmic and weak, subjective symptoms become less urgent ; he sleeps well now, he has no delirium at night, and he can take his food, and this although the body temperature may still range slightly above the normal. Then once more, and perhaps over and over again, fever with all the former symptoms gradually returns ; and now, if it has not declared itself before, the peculiar fleeting rheumatic-like affection of the joints or fasciæ, so characteristic of the disease, shows itself in a large proportion of cases. One day a knee is hot, swollen, and tender ; next day this joint may be well but another joint is affected ; and so this metastatic, rheumatic-like condition may go on until nearly all the joints of the body have been involved one after the other. The patient may suffer also from neuralgia in different nerves—intercostal, sciatic, and so on. Orchitis is an occasional complication. In some cases these complications are severe and

Digitized by Google

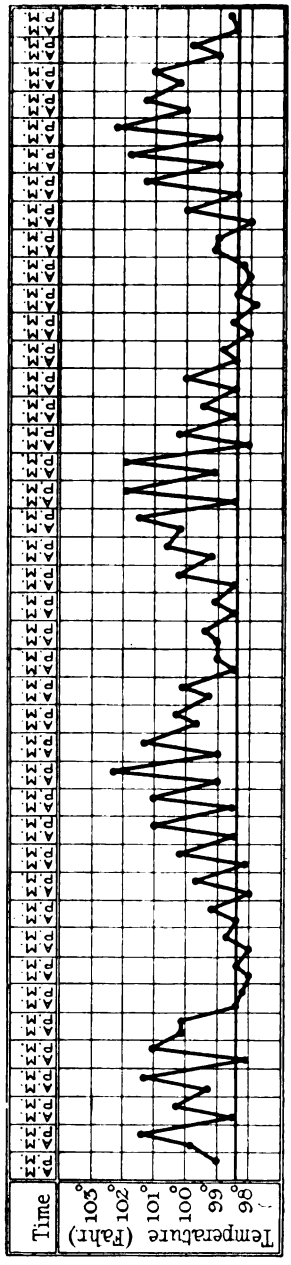


Chart 14.—Undulant fever. (*Bellingham-Smith.*)

characteristic; in others they may be mild, or absent altogether. In this respect the same infinite variety exists as in other specific fevers.

The most characteristic feature of undulant fever is the peculiar behaviour of the temperature (Chart 14). In a mild case there may be a gradual ladder-like rise through a week or ten days to 103° or 104° F., and then, through another week or so, a gradual ladder-like fall to normal, the fever, which is of a continued or slightly remitting type, leaving for good without complication of any sort in about three weeks. Such mild cases are the exception. Usually, after a few days of apyrexia, absolute or relative, the fever wakes up again and runs a similar course, the relapse being in its turn followed by an interval of apyrexia, which is again followed by another relapse; and so on during several months. This is the "undulant" type from which Hughes derived the name he suggested for the disease—*febris undulans*. A factor of practical importance from the diagnostic point of view is the tendency for the fastigium of the temperature curve to occur towards midday, or early afternoon (generally about 2 P.M.), a feature by which it may be distinguished from enteric, in which the maximum rise generally occurs towards 6 P.M., or from other long-continued septic fevers such as hepatic abscess, in which this takes place towards night-time.

In another class of cases a continued fever persists for one, two,

Digitized by Google

or more months, with or without the usual rheumatic, sudoral, and other concomitants—the "continued" type of Hughes.

Usually remittent or nearly continued in type, in a proportion of instances (generally paramelitensis infections) the fever exhibits distinct daily intermissions, the swinging temperature chart suggesting some septic invasion or a malarial fever. But there is no local evidence of suppuration to be found; neither, if we examine the blood, is the malaria parasite to be discovered; nor is the quotidian rise of temperature accompanied by any ague-like rigor, or at most only by a feeling of chilliness; nor is the disease amenable in any way to quinine. This is the "intermittent" type of Hughes. In other instances these types may be variously blended.

In some patients, not one month merely, but two to three may elapse before they are finally rid of the tendency to febrile attacks and characteristic pains and aches. According to Bassett-Smith, the average duration of the disease is four months. Many of our sailors and soldiers are permanently invalided from the services on account of prolonged or recurring attacks of undulant fever.

Sequelæ, complications, mortality.—As a rule, by far the most serious consequences of undulant fever are the debility it entails, the emaciation, the profound anæmia, the rheumatic-like pains, the neuralgias, and such sequelæ as abscess, orchitis, mastitis, parotitis, boils, etc. It is prone to give rise to ovarian pains, dysmenorrhœa, amenorrhœa, menorrhagia, and to favour abortion and premature labour. The germ may pass into the fœtus; children born under such circumstances are weakly.

Complications, such as splenic and hepatic enlargement, enlargement of the mesenteric glands, suppuration, phlebitis, chorea, various psychoses, arteritis, endocarditis, melæna, hæmaturia, etc., are met with occasionally during the long course of this disease. There is little risk to life; the mortality does not exceed 2·5 to 3 per cent. When death occurs it is usually from suddenly developed hyperpyrexia; occasionally it is brought about by exhaustion, by hæmorrhages and purpuric conditions, or by some pulmonary complication such as pneumonia. In a few instances the fever is of a fulminating type, rapidly ending in death from hyperpyrexia. Hughes, in his elaborate monograph, designates such cases "malignant."

Morbid anatomy and pathology.—This disease has almost no pathological anatomy. The spleen is the only viscus of which it can be said that it is distinctly diseased. In undulant fever this

Digitized by Google

organ is enlarged (average 17 oz.), soft, and diffluent; on microscopical examination the lymphoid cells are found to be increased in number. There may be some congestion and even ulceration of the intestinal mucosa, but this is not an essential feature. Other organs show chiefly cloudy swelling, and glomerular nephritis may be present.

Diagnosis.—The diagnosis of undulant fever from typhoid is an important practical matter. It is exceedingly difficult in the early stages. Principal reliance has to be placed on the characteristic temperature curve, the presence or absence of rose spots, of diarrhœa, of joint-complications, of sweats, the locality where and the season in which the disease was contracted, and, if available, the agglutination tests.

According to most authorities there is an increase of the lymphocytes to 40–50 per cent.; apart from this, microscopical blood examination, unless in a negative sense, is of no value in diagnosis.

Wright has shown that, both as regards sedimentation and agglutination, the germ of undulant fever reacts to the serum test in the same way as, and even more markedly than, *Bacillus typhosus*. A weaker dilution (never less than 1 in 30) than in typhoid may be used (*see* p. 902). Dead cultures give the reaction, and can be conveniently kept in stock for diagnostic purposes; they are grown on agar, washed off with sterile normal saline, killed by heat at 60° C. or by formalin vapour. These observations have been abundantly confirmed. The agglutination reaction appears early in undulant fever as compared with typhoid, being available for diagnostic purposes by the end of the first week of the fever. It persists long after convalescence, often for years.

The unreliability of the serum test for undulant fever as compared with that in typhoid has been explained by the researches of Nègre and Raynaud, who found that certain strains of *M. melitensis* agglutinated with normal serums, whereas other strains did not agglutinate with undoubted undulant-fever serums. The latter they name the "*paramelitensis* group." Bassett-Smith concurs in this. Therefore, before concluding from a negative reaction that any given case is not undulant fever, the serum should be tested with a *paramelitensis* culture.

Splenic puncture during life, and culture of the micrococcus from the material thus obtained, has been occasionally successfully practised.

Agglutination tests.—The microscopic agglutination test is not nearly so reliable as one performed by the macroscopic method. For this purpose the

Digitized by Google

serum, suitably diluted (1 : 50), is placed in sedimentation tubes with an emulsion of the organism, incubated at 55° C. for two hours, and placed on one side for a similar period to sediment. Young cultures should be used. The non-specific agglutinins may be destroyed by heating the suspected serum to 57° C. for half an hour.

This agglutination is also very readily performed by the *agglutination forcée* method (*see* Appendix, p. 898), but often remarkable inhibition zones occur—that is to say, the reaction takes place in the higher but not in the lower dilutions.

Bassett-Smith has procured a satisfactory complement-deviation with *melitensis*, using the micrococcus emulsion as an antigen.

After the fever has gone on for several weeks diagnosis is, of course, easier; in the early stages, on clinical grounds alone, and apart from the agglutination test, it may be almost impossible. It may be that it is only on the post-mortem table that we have the relative assurance, from the absence of ulceration in the ileum, that we have had to deal with a case of undulant and not typhoid fever. Cultures from spleen pulp, with subsequent inoculation into animals, should give reliable evidence if the results are positive. Tuberculosis, abscess, empyema, malaria, relapsing fever, and all the causes of continued high temperature of a septic type have to be carefully excluded in attempting a diagnosis. The possibility of the concurrence of another infection—typhoid, for example—must not be overlooked.

Prognosis.—In the present state of our knowledge it is impossible to say how long any given case of this disease may last, what the risk to life may be, or what complications may be encountered. Birt and Lamb, from a series of valuable observations, conclude that important inferences may be drawn from the behaviour of the agglutinating substances present in the blood. Their conclusions are, briefly, as follow: (1) Prognosis is unfavourable if the agglutinating reaction is persistently low; (2) also if the agglutinating reaction rapidly falls from a high figure to almost zero. (3) A persistently high and rising agglutinating reaction sustained into convalescence is favourable. (4) A long illness may be anticipated if the agglutination figure, at first high, decreases considerably. These conclusions are borne out by Bassett-Smith's very careful work.

Treatment.—Malta and those Mediterranean ports in which this fever is endemic should be avoided by pleasure- and health-seekers during the summer. Those who are obliged to live there all the year round would do well, at this season, to leave the towns and reside in places of healthy repute in the country. As a matter

Digitized by Google

of precaution, in the endemic areas the drinking-water, food, and drains ought at all seasons to receive special attention. *All milk should be avoided, or sterilized by boiling,* and food dishes should be washed with boiled water. Every care should be taken to avoid insect bites and other skin lesions. Laboratory workers must be careful in handling cultures of the micrococcus; the accidental introduction of the micrococcus into the conjunctival sac has sufficed to cause the disease.

When the diagnosis is sure, it is well to give a purge—none better than calomel and jalap—and to instruct the attendants to keep the patient's temperature systematically below 103° F. by cold sponging with vinegar and water or, if necessary, by cold bath or ice variously applied. In view of the prolonged nature of the fever, this measure is one of importance; at the same time, such treatment need not be applied too energetically, or so as to depress; a fall of 2° or 3° is all that is desirable.

Bassett-Smith recommends yeast and its products. Quinine and, on account of the joint affection, the salicylates are very generally prescribed. Both are useless, if not injurious. Phenacetin and similar antipyretics are also often given to bring down temperature; but the wisdom of employing depressing drugs in so chronic and asthenic a disease as undulant fever is, to say the least, questionable. Any threat of hyperpyrexia is best met as directed, namely, by early employment of sponging, the wet pack, or, if necessary, of the cold bath. Sleeplessness may demand hypnotics; headache, if severe, moderate doses of phenacetin, pyramidon, or similar drug; inflamed joints or testes, the usual local applications; constipation, enemata or aperients. In fact, the treatment of undulant fever resolves itself into a treatment of symptoms.

Vaccine-therapy.—The therapeutic use of vaccines of dead *M. melitensis*, prepared and administered according to Wright's methods, has been favourably reported on by Reid. In Bassett-Smith's hands sensitized vaccines have given the best results in doses of 100–250 millions. After a prolonged and careful trial, the latter concludes that if used during the acute phases of the fever, so far from doing good, they act detrimentally, but that in chronic cases, with slight relapses and low temperatures, by stimulating slightly the machinery of resistance they are of real value, and it is to this type of case that he now restricts their use. A considerable local reaction may occur after somewhat small doses of this vaccine. Recently Sergent has reported favourably upon inoculation with a dead vaccine, 800,000,000 micrococci per c.c., commencing with a dose of 0·25 c.c., followed by a second of 0·5 c.c. on the eighth day.

Digitized by Google

Serum-therapy.—Recently Sergent and Lhéritier have produced an anti-melitensis serum by intravenous inoculation of cultures into a horse. They say it is effective if given in doses of 50 c.c. on three consecutive days. It is useful in chronic as well as in acute cases.

The *diet* at first should consist of milk (in Malta, boiled); later of broths and eggs and, if necessary, stimulants. Solids must not be freely given during high fever or when the tongue is coated. If appetite is present, ordinary simple food may be taken. Lemonade or lime-juice should be given after a time; not merely as a pleasant, thirst-relieving beverage, but with a view to averting scurvy—not at all an improbable complication if the diet is too restricted over a long period. Feeding must be conducted with the greatest circumspection, avoiding overfeeding on the one hand, and a low monotonous diet on the other. The tongue and the appetite are the best guides.

Exercise, travelling, and anything that tends to induce fatigue are prone to provoke relapse if indulged in prematurely; but a couch or chair in the garden is to be encouraged, weather permitting. The patient should rest for at least three weeks after temperature has become normal.

Flannel clothing should be worn, and frequently changed if there is much sweating.

Change of climate is not so necessary as in malarial affections, seeing that the disease may persist in England, and that it may gradually wear out in the endemic localities. It is not desirable to move a patient when fever runs high, or when debility is very great, or when the cool and healthy season in the Mediterranean is at hand. It must be considered that at this time winter is approaching in England, with climatic conditions very unsuitable for a patient who has become anæmic and debilitated from a long course of fever: at this season he would do much better in a milder climate. When, however, the case occurs early in the summer, or runs over the winter, then, in order to avoid the heat of the Mediterranean, change to England, if feasible and if it can be comfortably effected, should be advised.

When possible the subject of undulant fever would do well to avoid the endemic area for one or more years after recovery. In chronic cases a change of climate would appear to be the only therapeutic measure of value.

Prevention.—Though mules, asses, oxen, cows, rabbits, and fowls can convey the micrococcus, there is no longer any doubt that goat's milk is the principal medium through which undulant

Digitized by Google

fever is communicated to man.* This discovery has led to very striking and important results.

On the recommendation of the Mediterranean Fever Commission, the use of the milk of the Maltese goat was interdicted in the naval and military forces of that island. Immediately the incidence of undulant fever began to drop in the Navy from an average of 240 per annum up to 1906, to 3 in 1910, and in the Army from a previous average of 315 per annum to 9 in 1907. In 1909 the health authorities in Malta were authorized to kill all goats whose blood or milk gave the *M. melitensis* reaction. The goat population of the island was consequently reduced from 17,110 in 1907, to 7,619 in 1910. Concurrently the fever incidence in the civil population fell from an annual average of 632 to 318 (Eyre).

These facts suffice to indicate the direction preventive measures should take. It must be borne in mind that certain products of milk—cheese, butter, etc.—may communicate the germ, and, further, that infected goats may appear to be in perfect health and may milk satisfactorily.

* The proportion of infected goats has been estimated as follows:—

Malta	50 per cent.
Algeria	3·4 ,,
Tunis	30·7 ,,
Marseilles	34·2 ,,

Digitized by Google

CHAPTER XXI

ENTERIC AND ENTERIC-LIKE FEVERS IN THE TROPICS

THE existence of the enteric fevers in the tropics was for long not only ignored, but actually denied, even by physicians and pathologists of repute. Formerly, the idea of malaria so dominated all views of tropical fevers that nearly every case of pyrexia, other than those of the most ephemeral description, or those associated with the exanthemata or with manifest inflammation, was relegated to this cause. When ulceration of the ileum was encountered post mortem the lesion was regarded, not as the specific lesion of the fever, but merely as a complication. More correct views prevail at the present day, and enteric now ranks not only as a common disease in the tropics, but, to the European there, as one of the most commonly fatal. Probably the enteric fevers are not so widespread or so virulent in natives as in Europeans, but since the advent of more exact laboratory methods they are known to occur.

Besides being the scourge of the young European in India, enteric is common enough in Japan, in China, in Cochin China, in the Philippines, in the Malay country, in Mauritius; the French have had large experience of it in Algeria and their West African possessions; the British have had similar experience in South Africa. It is also found in the West Indies; in Nigeria and East Africa even; in fact, wherever it has been properly looked for. Thanks to protective inoculation with the triple vaccine (T.A.B.) during the War, enteric fever was no longer the chief disease factor in our armies. Since 1904 it has been recognized that a considerable proportion of enteric fevers in the tropics are really infections with either paratyphoid-A or -B.

Propagation.—Enteric fever is prevalent among young soldiers and civilians in the East. It is very common among them during the first two or three years after their arrival. Fortunately, the liability decreases with length of residence. Apparently a sort of acclimatization, or rather habituation, to the poison is established with time, just as tends to be the case with other organic poisons. It is not unlikely that the relative exemption—if such there be—of the native races is owing to a like immunizing effect produced by living in constant contact with typhoid and similar toxic agents,

Digitized by Google

or to an attack in childhood. On visiting native cities—Chinese, cities, for example—one is filled with amazement at the state of filth in which the people live, and not only live but thrive. The streets are narrow and never cleansed; the common sewer lies beneath the flagstones, and through the interstices between the stones can be seen the black, stinking slush in the sewer. The sewage is not confined in a well-laid cemented drain, but soaks through the loosely laid, uncemented stones, and thoroughly saturates the ground on which the tumble-down, overcrowded houses are built. In every corner are filth and rubbish. And yet in such circumstances the population seems to thrive! Doubtless, where the European would almost surely contract typhoid and other filth diseases, the natives have obtained a high degree of immunity.

In Eastern countries little or no care is taken to prevent contamination of the wells and streams with sewage matter, and unless foreigners are very careful about boiling their drinking-water and the water in which food-dishes, etc., are washed, avoiding salads and all uncooked vegetable dishes, refraining from bazaar-made drinks, and protecting their food and food-dishes from flies and other mechanical transmitters of the *Bacillus typhosus*, they are almost sure, sooner or later, to fall victims.

It would appear that typhoid and paratyphoid are not only common among Europeans in the tropics, but that they are also very virulent, with a death-rate twice as heavy as the death-rate of typhoid in England. In England the death-rate is put down as about 1 in 8 attacked; but in India, until recent years, the elaborate and carefully prepared statistics show a death-rate of rather over 1 in 3. Typhoid in India, indeed, used to kill more European soldiers than cholera.

Not only does enteric exhibit increased virulence, but experience has shown that against it those sanitary safeguards which are found to be practically sufficient in England are by no means so effective in the Indies. It would also appear that soldiers on the march contract the disease in passing through uninhabited country, in spite of the fact that the camp may be pitched in spots which, presumably, had never been occupied by man before, and although the men may have drunk only of water from springs and streams that were beyond suspicion of fæcal contamination. Similar testimony comes from Australia, where typhoid has occurred in the back country in lonely spots hundreds of miles from fixed human habitations. These data suggest that typhoid carriers are more numerous and varied than is generally believed, or that Eberth's bacillus, under certain conditions of soil and temperature, may exist as a pure yet

Digitized by Google

virulent saprophyte, for which an occasional passage through the human body may or may not be necessary. Since the early days of the recent war it has been suggested that the term "enterica" should include both typhoid and paratyphoid infections.

Etiology.—The essential factor in the propagation of enteric fevers in the tropics, as in temperate climates, is the individual who is passing enteric bacilli in his excreta (urine or fæces, or both). He may be in the acute or the convalescent stage, or a "carrier." Three kinds of enteric carriers are alluded to by writers on this subject. (*a*) The *acute carrier*, the person who passes enteric bacilli in the excreta for a short period after an attack of enteric fever. (*b*) The *chronic carrier*, who continues to pass enteric bacilli in the excreta for years, possibly permanently. Chronic carriers are more often women than men; the gall-bladder is the seat of a chronic infection, the carrier sometimes suffering from gall-stones and cholecystitis. (*c*) It is believed by some that a person may pass enteric bacilli in the excreta without having at any time previously suffered from an attack of enteric fever. Such a person is called a *passive carrier*.

The enteric carrier is a source of danger to the community, the degree of danger depending to some extent on his personal hygiene, but much more on the sanitary state of the locality. Under an efficient water-carriage system of sewage disposal there is a minimum risk of the carrier conveying infection to others. Where the conservancy system—i.e. the dry closet—is employed, as in the tropics generally, the risk of infection is great. The modes of infection are: (1) directly from the infected person (patient or carrier) to the susceptible individual, (2) indirectly through water supply, and (3) indirectly by fly-carriage and contamination of food. When one considers these sources and modes of infection, and reflects on the primitive sanitary development of tropical countries, the amazing state of filth in which the native population live, and the almost constant plague of flies, it is not surprising to learn that enteric fever is one of the commonest and most widely distributed fevers of the tropics. It is undoubtedly the biggest health risk the European entering the tropics has to face. Fortunately this risk can be greatly diminished, or practically abolished, by prophylactic inoculation with a mixed typhoid and paratyphoid vaccine before leaving for the tropics—and re-inoculation with the same vaccine yearly.

Bacteriology and pathology.—In the earlier half of the nineteenth century typhoid and typhus fever were grouped together under the term "continued fever." The first clear differentiation

Digitized by Google

of typhoid from typhus on clinical and pathological grounds resulted from the work of Murchison and Jenner at the London Fever Hospital (1855–62). Then came the discovery of the *Bacillus typhosus* by Eberth in 1881, followed by that of *B. paratyphosus-A* (Brion and Kayser), of *B. paratyphosus-B* (Schottmüller), and of *B. paratyphosus-C* (Hirschfeld, 1919). "Enteric fever" applies therefore to a group of four diseases, and further research may lead to the discovery of other members of this family. In addition to these, *B. fæcalis alkaligenes* is an intestinal organism which may enter the bloodstream and produce a continued fever closely resembling enteric.

The portal of entry of the enteric bacilli into the tissues of their host would appear to be the lymphoid masses forming the Peyer's patches and solitary follicles of the ileum. Here they cause a hyperplasia of the lymphoid tissues, followed at a later stage, in severe cases, by necrosis, sloughing, and ulceration. The bacilli pass on to the lymphatic glands of the mesentery and posterior abdomen, which become enlarged. Finally they enter the bloodstream. The period of bacillæmia coincides with the early febrile stage of the disease, and hæmoculture by appropriate methods is successful in the majority of cases in which it is undertaken sufficiently early—i.e. while the temperature is still rising, or when it is continued without marked remissions. It is seldom successful after the first marked morning remission, especially in paratyphoid fever, or after lysis has commenced. The duration of bacillæmia varies greatly and depends on the severity of the case and duration of the pyrexia. It is, on an average, longer in typhoid than in the paratyphoid fevers. It is important, therefore, to undertake hæmoculture as early as possible in the diagnosis of enteric fever; every day's delay diminishes the chance of success.

Another conception of the pathology of the enteric infections is that the invading organisms enter the bloodstream first (possibly through the tonsils), and that the intestinal lesions are secondary to the bacillæmia.

Although bacilli are eliminated from the body in the fæces and urine, it is only in a small proportion of cases that they are isolated from the excreta, even on repeated examinations.

Description of organisms.—B. typhosus is a Gram-negative motile rod, 2–4 μ in length and 0·5 μ in thickness. It is provided with numerous peritrichous flagella and is very active when grown on artificial media. On these it thrives well, with a growth resembling that of *B. coli*, but less dense. In its biochemical reactions it differs considerably from that organism, and produces acid

Digitized by Google

without gas-formation in maltose, glucose, and mannite, but causes no change in lactose, saccharose, and dulcite. It produces slight acidity in milk without clotting. No indol is produced in peptone water (*see* Table p. 408). The paratyphoid bacilli A, B, and C resemble in their general morphological characters and staining reactions *B. typhosus*, but differ from it in their biochemical and immunity reactions. They also, like *B. typhosus*, are non-lactose-fermenters, but produce acid and gas in glucose, mannite, maltose, and dulcite, but do not affect saccharose, nor do they form indol in peptone water. The "A" bacillus is weaker in fermentative power than "B," and it produces permanent acidity in litmus milk, while "B" first produces acid, returning later to a permanent alkaline reaction. Their immunity reactions are also quite specific. The "C" bacillus differs from "B" only in its immunity reactions, and some bacteriologists might prefer to call it a serological race of "B."

Post-mortem appearances.—The most striking lesions found post mortem (in addition to the tissue changes common to all continued fevers) are—

(1) Ulceration of the intestine, especially the Peyer's patches and solitary follicles in the ileum and jejunum.
(2) Enlargement and congestion of the abdominal lymphatics.
(3) Enlargement and congestion of the spleen.

The most notable differences in the post-mortem appearances between typhoid and the paratyphoid fevers are—

(1) In paratyphoid fevers the intestines more frequently show no change.
(2) In paratyphoid fevers the intestines may be acutely inflamed throughout their length, the lymphatic tissue escaping.
(3) In paratyphoid fevers ulceration of the *large* intestine is relatively more frequent.

Post-mortem bacteriology.—The causative organism in enteric fevers may be recovered post mortem from—

(1) The intestinal lesions.
(2) The enlarged abdominal lymphatics.
(3) The spleen.
(4) The gall-bladder.
(5) The heart's blood.
(6) Other tissues of the body.

Epidemiology.—*B. typhosus* is practically worldwide in its distribution. Paratyphoid-A fever is the most common infection

Digitized by Google

in the East (India, etc.), while paratyphoid-B fever prevails in Europe. This distribution, however, is not absolute, for "A" infections occur in Europe and "B" infections in the East. During the recent War the majority of enteric infections in France were paratyphoid-B. The greatest enteric epidemic was that among the British and French troops on the Gallipoli peninsula in 1915. There were relatively very few cases of typhoid in this epidemic, the armies being almost completely protected by anti-typhoid inoculation. In the earlier part of the epidemic paratyphoid-B was the prevailing infection, while in the later phases the cases were almost exclusively paratyphoid-A. Paratyphoid-C fever has probably not the epidemiological importance of the other three fevers; otherwise it would have been discovered earlier. It has so far been reported from Macedonia (where it was first discovered by Hirschfeld), from Mesopotamia by Macadam, Mackie, and Bowen, from India by Kennedy, and one case has been reported from East Africa by Garrow. The disease, therefore, although it is more closely allied to para-B fever, has a distribution more like that of para-A.

Symptoms.—The usual incubation period for all the enteric infections is about fourteen days, but it may be shorter than seven or longer than twenty-one days.

There is a wide range in the severity of the infections, and it will be readily understood that one clinical description cannot apply equally to all cases, from the mildest to the most severe. Nevertheless, the variation is more in the degree than in the nature of the clinical manifestations. In spite of all that has been written, especially during the War, on "atypical" enteric fever, this group remains, whether in inoculated or uninoculated patients, remarkably true to one type—which may be termed the "enteric type."

The classical *onset* is gradual, but it may be sudden, with a shiver or even a rigor, especially in paratyphoid fever. Headache is the most constant early symptom and is usually accompanied by malaise, anorexia, pains throughout the body and limbs, and insomnia. The tongue is coated, the mouth dry and uncomfortable, and the patient is thirsty. There is a characteristic moist facies with cheek-flush, and a general apathy. These symptoms vary greatly, and in the mildest cases may pass undetected. Epistaxis is more common in typhoid than in paratyphoid. There may be pain or general uneasiness in the abdomen, but in mild paratyphoids the patient in many cases does not refer to that region. There may be diarrhœa from the commencement, or diarrhœa followed

Digitized by Google

in a few days by constipation, or the patient may have obstinate constipation from the beginning. The temperature is invariably raised. It may mount stepladder-like during the first week, or it may rise suddenly, to reach its highest point in the first 24–48 hours and, after a phase of continued fever, begin to remit in the morning, and terminate by lysis. (Chart 15.) A highly characteristic feature of all the enteric infections is the pulse, which is usually soft, often dicrotic, and relatively slow.

On physical examination, the abdomen may be found to be more or less distended, as in severe typhoid, or there may be little or no distension, as in the majority of paratyphoids. Splenic enlargement is practically a constant feature of enterica. The spleen

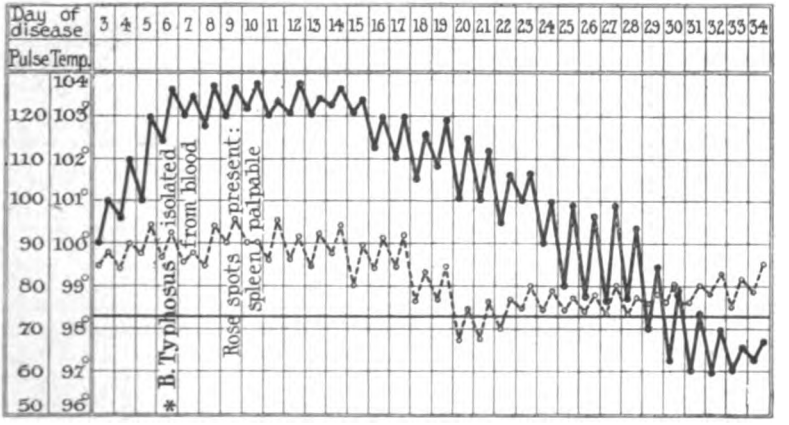


Chart 15.—Typhoid fever, with graph of pulse-rate. (*Garrow.*)

usually enlarges sufficiently to render its lower pole palpable below the left costal margin at some stage of the illness. It may be felt in some cases on the second or third day, if the patient comes under observation so early, or it may not be palpable till the second or third week, or even later. In some cases it becomes palpable for the first time only after the temperature is normal. Usually about the seventh to the tenth day, but it may be earlier or much later, "rose spots" appear. These vary considerably in number, size, shape, general characters, and distribution. There may be only two or three on the abdomen, or the body and limbs may be covered from the soles of the feet to the scalp. They are of a pale-rose colour, slightly raised, round or lenticular, and fade on pressure. The more profuse eruptions occur in paratyphoid

Digitized by Google

fever, especially para-A. When the eruption is not of this profuse type its distribution is characteristic; 90 per cent. or more of it is on the trunk, between the levels of the iliac crests and the

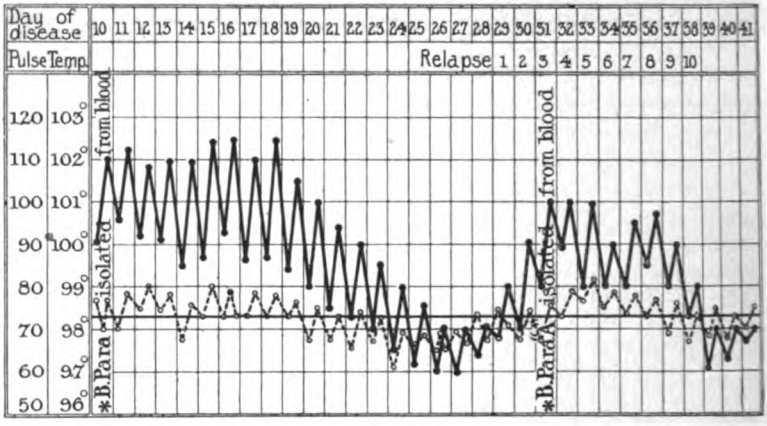


Chart 16.—Paratyphoid-A fever, with graph of pulse-rate. (*Garrow.*)

nipples. The patient usually coughs and has a certain degree of bronchitis. (Charts 16, 17.)

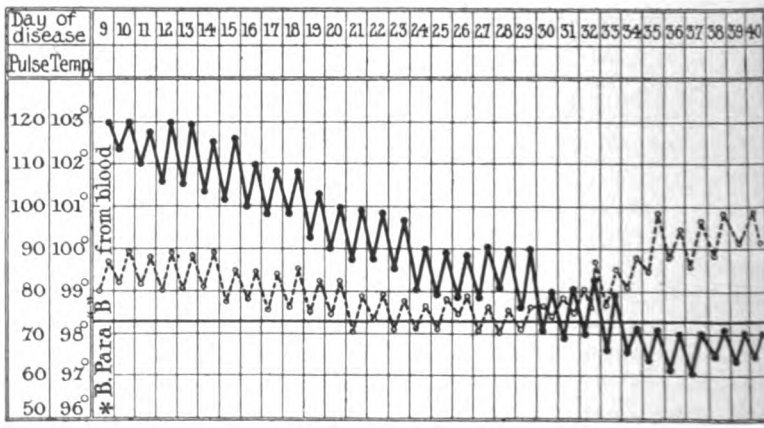


Chart 17.—Paratyphoid-B fever, with graph of pulse-rate. (*Garrow.*)

Clinical diagnosis.—In the literature of enteric there is frequent reference to mild, atypical, abortive, and clinically unrecognizable forms; and it appears to have become the custom to leave

Digitized by Google

the question of diagnosis to the laboratory. This was particularly so during the War, both at home and abroad, and it is greatly to be deprecated, because careful and repeated clinical scrutiny of these cases is more than ever necessary. It is Garrow's opinion that the great majority can be correctly diagnosed clinically. While laboratory methods of diagnosis in the enteric group are undoubtedly important, undue value has been attached to certain bacteriological and serological findings, even to the extent of creating new clinical types of the disease to correspond to them. Far from being protean in their clinical manifestations, the enteric

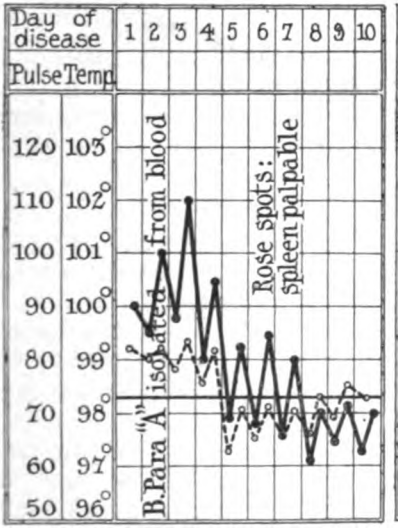


Chart 18.—Anomalous paratyphoid-A fever. (*Garrow.*)

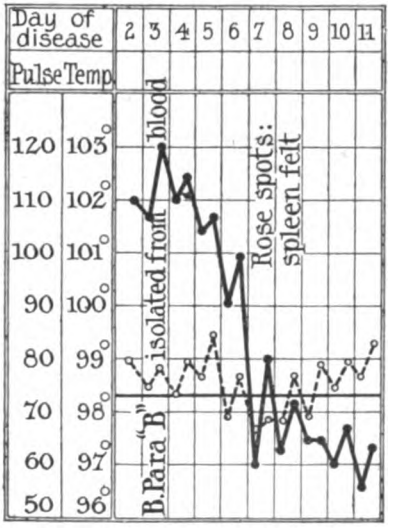


Chart 19.—Anomalous paratyphoid-B fever. (*Garrow.*)

fevers are remarkably constant and true to type. The cardinal signs of this type are five in number:

(1) Continued pyrexia of remittent type ending by lysis; (2) low pulse-temperature ratio; (3) characteristic toxæmia; (4) splenic enlargement; (5) eruption of rose spots. It is not pretended that this list exhausts the diagnostic signs and symptoms; but a consideration of these five signs will, in the great majority even of the milder cases, lead to correct diagnosis. (Charts 18, 19.)

(1) *Pyrexia.*—Continued pyrexia of remittent type, ending by lysis, may be regarded as a feature of every case of acute enteric

Digitized by Google

fever (typhoid or paratyphoid). The pyrexia may be high or low, long or short, with remissions great or small. The onset of pyrexia may be gradual or sudden, and lysis may be slow or rapid, thus giving a great variety of temperature charts within the type. But there is no good evidence to show that fever ever departs from this type. *Cases presenting the following features certainly should not be regarded as enteric.*

(*a*) Temperature normal or subnormal throughout the entire illness ("apyrexial type of enteric").

(*b*) Temperature reaches normal or subnormal at some period of the twenty-four hours on every day of the illness ("intermittent type of enteric").

(*c*) Temperature shows perfect tertian or quartan periodicity throughout ("malarial type of enteric").

(*d*) Temperature shows a series of short relapses of one to three days' duration, occurring at intervals of a few days ("trench-fever type of enteric").

(*e*) The temperature ends by a genuine crisis.

Examples of all these so-called "types of enteric fever" will be found in the literature, the erroneous diagnosis having been based upon some bacteriological or serological finding.

(2) *Low pulse-temperature ratio.*—One of the most valuable diagnostic points is the slowness of the pulse in relation to the pyrexia. The normal pulse-temperature ratio may be thus tabulated :—

Pulse . . .	50	60	70	80	90	100	110	120	130	140
Temperature .	96°	97°	98°	99°	100°	101°	102°	103°	104°	105°

In enteric fever the pulse is, as a rule, 20 or 30 or 40 beats per minute slower than that indicated. For example, it is common to find an enteric patient with a temperature ranging about 103° to 104° F., and a pulse of 90 beats per minute, or it may be even slower. If the pulse is recorded graphically in red ink alongside the temperature curve in black, a very striking clinical feature of great diagnostic significance is clearly brought out.

(3) *Characteristic toxæmia.*—There is something very characteristic in the general appearance, facies, and decubitus of the enteric-fever patient. The disease may in many cases be confidently diagnosed by a glance at him as he lies in bed. He has a dull, heavy, toxin-laden appearance in the early acute stage of his disease, with a moist face and flushed cheeks. The experienced clinician at once recognizes the difference between this and the toxæmia of, say, malaria or relapsing fever. On the other hand,

Digitized by Google

it must be remembered that in the mildest paratyphoids there is little or nothing of this toxic appearance, and some infections other than enteric are accompanied by a general toxæmia closely resembling that of enteric fever. This sign, nevertheless, when taken in conjunction with the others, is of great diagnostic significance to the experienced physician.

(4) *Splenic enlargement.*—Some degree of splenomegaly is practically an invariable feature of enteric fever, and this sign is of considerable value in contributing to a diagnosis. Unlike the majority of tropical splenomegalies from other causes (malaria, kala-azar, etc.), the enlargement is acute, so that, even when superadded to a spleen already enlarged from malaria, it has certain features of diagnostic significance. For example, the acutely enlarged spleen of enteric is tender. On palpation the edge of the spleen seldom comes more than two fingers' breadth below the costal margin, and often not so much as this; and the enlargement is of comparatively short duration. The spleen may be palpable only for two or three days, and then recede. It may become palpable as early as the second or third day of fever, or not till the second or third week, and it may remain enlarged long into convalescence.

(5) *The eruption of rose spots.*—These may appear in the first week, but more often in the second, and they tend to come in crops. They may not erupt till the temperature is normal. In warm climates, many European skins are apt to show spots more or less like those of enteric fever—caused by mosquito bites and by inflammation of hair-follicles, sweat-glands, etc. Great care must be taken in discriminating between the true rose spot and these "pseudo-rose spots," but there are many European skins which, in spite of the trying conditions of the tropics, remain free from blemishes of this sort, and in these cases the recognition of rose spots is relatively easy. Due regard must be paid to the type of skin.

Summary of clinical diagnosis.—Every undiagnosed fever in the tropics should be regarded as a possible case of enteric fever and closely observed clinically, at the same time that bacteriological and serological investigations are being carried out and Marris's atropine test is applied. While valuable clinical evidence may be obtained from occasional signs such as epistaxis, pea-soup stools, abdominal distension, and hæmorrhage from the bowel, the diagnosis should rest in the great majority of cases upon the presence or absence of the five cardinal signs above described. Any case presenting the first, second, and third signs should be treated as

Digitized by Google

enteric (whether the diagnosis is supported by laboratory findings or not) until some other definite diagnosis is arrived at. No case which does not show the first together with at least two of the remaining four cardinal signs should be finally regarded as enteric. Five types of temperature chart are mentioned, any of which excludes enteric. These, however, imply that the case has had its temperature recorded from the first, which is not often possible. In the majority of cases of active enteric fever, all five signs are presented at one or other stage of the illness.

Finally, it should be remembered that, for every case of enteric fever which imitates some other disease, there are at least a score of cases of other diseases imitating enteric (malaria, trench fever, phthisis, liver abscess, syphilis, etc.).

Bacteriological diagnosis.—(*a*) *Hæmoculture* is unquestionably the most satisfactory method of diagnosis, and should be employed, where facilities exist, in every case of undiagnosed pyrexia in the tropics so soon as a blood-film is found to be free from malaria parasites. A successful hæmoculture furnishes the only conclusive evidence that the patient is suffering from active enteric fever, and can hardly be said to be open to fallacy. Unfortunately, however, the usefulness of the method is limited by the short duration of bacillæmia. In many cases which are undoubtedly enteric negative results are obtained because hæmoculture has been attempted too late.

(*b*) *Culture of excreta.*—The plating of specimens of urine and stools should be undertaken in cases in which blood-culture has failed to give a diagnosis, and should be repeated during convalescence to determine whether the patient is free from infection. This routine method involves a great deal of work for relatively few positive findings. Bacilluria occurs generally after the fourteenth day, and in about 15–20 per cent. of the cases, and, as a general rule, cultivation from fæces will only succeed in about 5 per cent. of the cases in which it is attempted. It must be borne in mind that positive findings from culture of excreta are open to fallacy. The case may be one of an enteric carrier suffering from some illness other than enteric—e.g. malaria, or trench fever. The detection of carriers can only be effectually carried out by employing the resources of a fully-equipped laboratory; at least seven separate and consecutive bacteriological fæcal tests are necessary. These methods are more adequately dealt with in Appendix III. p. 903.

Serological diagnosis.—One of the simplest and most reliable of laboratory tests is the examination of the blood-serum of sus-

Digitized by Google

pected enteric-fever patients for the specific agglutinins of the enteric bacilli—the *Widal reaction*. When carefully applied by reliable methods in the case of *uninoculated patients* it leads to a correct diagnosis in the great majority of cases. Assuming correct technique, the only possible fallacies are that a positive Widal reaction may result from a *previous* attack of enteric; and that a negative result may occur in the early stage of an attack of enteric. If a negative finding is obtained in face of clinical data pointing to enteric, the test should be repeated, on several occasions if necessary. A few cases of enteric, especially paratyphoid-A, may fail to develop agglutinins and continue to give a misleading negative Widal reaction throughout.

The serological diagnosis of the enteric fevers in *inoculated patients* is a difficulty which gave rise to much conflict of opinion during the War. Inoculation produces in the blood-serum specific agglutinins indistinguishable qualitatively or quantitatively from those produced by infection. The mere recognition of these specific substances has not, therefore, the diagnostic significance in the inoculated that it has in the uninoculated. It has, indeed, hardly any diagnostic value. It was, however, demonstrated by Dreyer and his co-workers, and by others, that if an accurate estimate of the agglutinin content of the serum is made as early as possible in enteric fever, and repeated at intervals of a few days, there is a steady rise to a maximum, followed by a slower fall. Dreyer and Walker stated that this maximum usually occurred between the eighteenth and twenty-first day of the illness, and almost invariably between the sixteenth and twenty-fourth day. To this latter period they therefore gave the name "period of expectation." To this agglutinin fluctuation they attached a significance practically pathognomonic. Unfortunately their claims are not borne out by the published cases. While the method is undoubtedly of value, the results obtained are often very difficult to interpret, and misleading. Some undoubted cases of enteric fail to give this fluctuation, while some cases of fevers shown conclusively not to be enteric give a characteristic rise and fall in the inoculation agglutinins. The truth probably is that the majority of enterics give a fluctuation and the majority of fevers not enteric do not. Thus the agglutinin fluctuation, when considered in relation to the clinical data, is useful, but it should not in itself be regarded as conclusive.

Diagnosis by the Marris atropine test.—The most important contribution made during the War to the diagnosis of enteric fevers is the atropine test devised by Marris. Its great

Digitized by Google

advantages are its simplicity and reliability. It does not, however, give a differential diagnosis between typhoid and the paratyphoid fevers, all cases in this group responding to the test in the same way. It depends on the fact that, in health or disease other than enteric fever, hypodermic injection of atropine sulphate, gr. $\frac{1}{50}$ to gr. $\frac{1}{33}$, is followed by a rise in pulse-rate amounting to at least fifteen beats per minute, usually much more; whereas in the enteric patient no such rise follows. If there be any rise at all, it is less than fourteen beats per minute, but often there is none, and there may actually be a fall.

The test is applied thus:

"The patient lies horizontally and is instructed to remain completely at rest throughout the test, which is not employed until at least one hour has elapsed from the last meal. The pulse-rate is counted minute by minute until it is found to be steady; ten minutes of such counting usually suffices. Atropine sulphate is then injected hypodermically in the dose of $\frac{1}{33}$ gr., preferably over the triceps region to ensure rapid absorption. An interval of twenty-five minutes is allowed to elapse, and the pulse is again counted, minute by minute, until it is clear that any rise which may have followed the injection has begun to pass off; fifteen to twenty minutes may be necessary for this purpose when the pulse-rate is raised at the first count" (Marris).

Of the diagnostic value of the test Marris says:

"In my own experience, which at any rate has been wide, the test is most serviceable. The test is serviceable not only because of its unusual reliability, but for several other reasons. The method involves little or no expense. The tests are carried through quickly and yield their answers expeditiously. In these particulars the test fulfils the chief needs of the clinician in dealing with suspect cases of typhoid; the test is especially competent under war conditions and with patients who almost without exception have been previously inoculated, and in whom the disease and the serological reactions are in consequence profoundly modified. *The test is standardized.* The technique is so simple that it may be applied successfully by assistants, after a very short period of instruction. It is my personal conviction that there is no test, clinical or pathological, which approaches the atropine test in speed, simplicity, and reliability for sorting inoculated patients suspected of enteric into two groups of 'enteric' or 'not enteric.'"

Evidence is accumulating to show that this claim is justified. The great boon of such a test to the tropical practitioner is obvious.

Explanation of atropine curves.—The two curves in Charts 20, 21 show the pulse-rate for ten minutes before and fifty minutes after an injection of $\frac{1}{33}$ gr. of atropine sulphate. The upper curve is from a person in perfect health, the lower from a patient on the sixteenth day of an attack of typhoid fever. In each case the average pulse-rate before the hypodermic administration of atropine was 85, as seen at A. The atropine was given at B, and a record of the pulse kept for fifty minutes. In the healthy person the pulse-rate fell steadily during the first ten minutes to 70. Thereafter it rose steadily and

Digitized by Google

reached a maximum of 120 about thirty-three minutes after the injection. The difference between 85 and 120 represents an "escape" or acceleration of 35—i.e. a "negative" result. In the lower curve the "escape" is very small, not more than four or five beats per minute, which represents a well-marked positive atropine reaction for enteric. It is not necessary to keep a

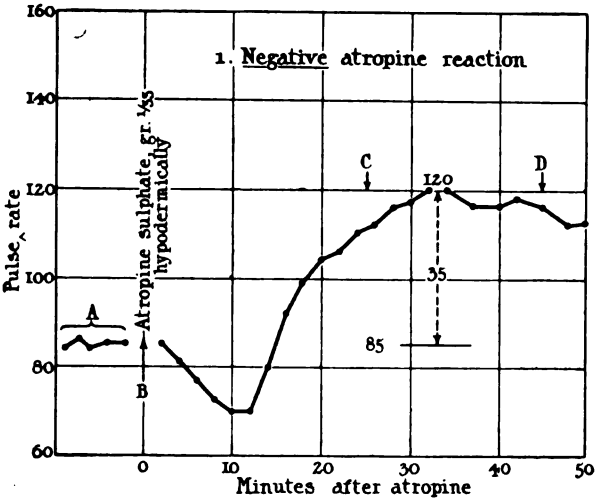


Chart 20.—Illustrating a negative atropine test.

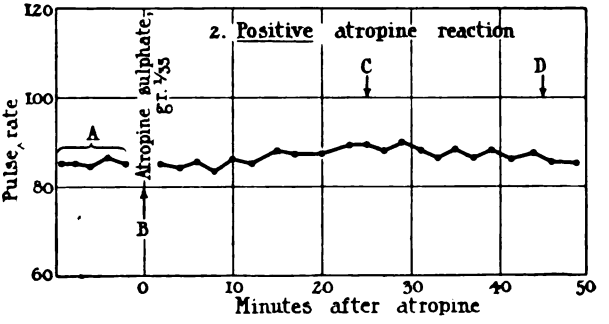


Chart 21.—Illustrating a positive atropine test.

continuous record of the pulse after the atropine injection. Marris directs that an interval of twenty-five minutes be allowed to elapse—i.e. begin counting at C, and count till the acceleration ceases or begins to pass off as at D. Marris draws the line between a negative and a positive reaction at an acceleration of 14. If under 14 it is regarded as positive, if over 14 as negative, for enteric fever. In doubtful cases the test may be repeated. The period of the disease during which the test is most reliable is from the fifth day to

Digitized by Google

the end of the second week. From the fourteenth day onwards its reliability undoubtedly decreases.

As an accessory means of diagnosis, the *diazo reaction* in the urine (p. 908) is useful. It may be present in malaria. On the other hand, Russo's methylene-blue test is said to be more conclusive, as it is absent in malaria, though it may be present in measles and smallpox.

Diagnosis from other diseases.—Almost every other disease attended by fever may be mistaken for enteric, but even in the most perfect imitations a careful application of the diagnostic methods just discussed should lead to a correct diagnosis in the great majority of cases. The experienced and alert physician need never miss a case of enteric fever, provided he is given reasonable opportunity. Nor should the elimination of other diseases imitating enteric present insuperable difficulties. A careful, systematic physical examination of every organ and region of the body, together with macroscopic and cultural examination of the blood, sputum, urine, fæces, and other discharges, will furnish evidence of malaria, trypanosomiasis, relapsing fever, pneumonia, tuberculosis, liver abscess, syphilis, malignant disease, worm infection, or other pathological condition. It is only by comprehensive and sustained effort along these lines that the many puzzling pyrexias of tropical countries can be unravelled and correct diagnosis arrived at. And even when no definite label can be attached, it is often possible to say that the case is not enteric. Diagnostic defeats may be relegated to that rubbish heap of military medicine, namely, "P.U.O." (Pyrexia of Unknown Origin).

The abdominal pain of enteric may be mistaken for appendicitis, but the matter may be easily settled by a leucocyte count, which in the former is a leucopenia with a relative lymphocytosis, and in the latter an active leucocytosis. *Bacillus coli* infections may resemble enteric. Typhus is notably difficult to distinguish in its earlier phases; the leucocytosis which is present in that disease will be found of considerable assistance.

It must not be forgotten that enteric fever may coexist with some other acute infection.

Diagnosis of typhoid from paratyphoid.—There are no *clinical* features which serve to distinguish the typhoid and paratyphoid infections from one another with any certainty. Yet there are general points in which they differ. Thus, typhoid fever (*B. typhosus* infection) is the most severe fever of the group, with the highest case-mortality (15 per cent. or over, as compared with 2 per cent. or less for the paratyphoid fevers). The typhoid

Digitized by Google

patient looks more toxic, his temperature is, on an average, higher, with smaller morning remissions ; he more frequently shows evidence of gross intestinal lesions (ulceration), e.g. diarrhœa, hæmorrhage, abdominal distension, perforation. The rash is more scanty and the individual "rose spots" are smaller and slightly darker in hue than in paratyphoid. There is greater loss of flesh in typhoid than in paratyphoid. Paratyphoid is characterized by a milder toxæmia. There is seldom abdominal pain or distension, and constipation is the rule. Hæmorrhage and perforation are rare. The rash is more profuse and may cover the entire body and limbs.

But typhoid is frequently of the very mild type, and, on the other hand, paratyphoid may be like the worst typhoid. It is therefore quite impossible to say on clinical grounds alone whether any individual case is one of typhoid or paratyphoid.

Still less is it possible to arrive at a differential diagnosis on clinical grounds between "A," "B," and "C" cases of paratyphoid, although here again, over a series of cases, distinct clinical differences can be noticed. For example, relapses in paratyphoid-A are more frequent than in any other of the enteric infections, and less frequent in paratyphoid-B. Para-A is, on an average, of longer febrile duration than para-B, but the latter, on the other hand, is more often followed by jaundice, thrombosis, and suppurative complications.

Bacteriological.—The most satisfactory differential diagnosis between the different fevers of the group is the isolation of the causative organism from the blood or excreta, and its identification.

Serological.—In uninoculated patients differential diagnosis is obtained by carrying out agglutination tests with the patient's blood-serum against emulsions of the four organisms concerned. Each infection produces its specific agglutinin, and the phenomenon of co-agglutination does not often interfere with the diagnosis. In patients who have been inoculated with triple vaccine the problem of differential diagnosis is considerably complicated. The response may be specific, but frequently two or all three agglutinins may show variations.

Prophylaxis.—*Anti-enteric inoculation* is conspicuously successful, as shown by the statistics of the American Army, and of the British Army in India. During the War the vaccine was modified by the introduction of *B. paratyphosus-A* and *-B*, and the statistics furnish conclusive evidence of the efficacy of this measure of prevention, not only in preventing the incidence of the disease or diseases, but also in modifying the course in those exposed to infection after inoculation. Therefore everybody pro-

Digitized by Google

ceeding from a country like England to the tropics or subtropics should be inoculated with two doses of triple vaccine (T.A.B.), and should be re-inoculated every year subsequently with one dose, so long as he remains in a country where enteric is prevalent.

The typhoid vaccine, as originally introduced, caused a considerable reaction, but by better methods of preparation and dosage in recent years the reaction has been mitigated. It is better to use a reliable standardized vaccine not over three months old, and to give two doses, the first containing 500 million (or 0·5 c.c. of emulsion); the second, ten days later, containing 1,000 million bacilli (1 c.c.).

The triple vaccine is protective both against typhoid and paratyphoid, and was utilized on a large scale during the War. The official vaccine contains 1,000 millions of typhoid bacilli, 750 millions of paratyphoid-A, and an equal number of paratyphoid-B to each c.c. Two doses of 0·5 c.c. and 1 c.c. are given at an interval of ten days. The reaction it causes is, in the majority of instances, very slight. Occasionally, however, cases of persistent pyrexia with severe local symptoms, malaise, and headache are met with.

Preparation of the vaccine.—The organisms are grown upon trypsin-agar, washed off in saline and killed by heat. The vaccine is then standardized by combining the various bacterial suspensions in their appropriate proportions. The final emulsion is preserved by the addition of 0·4 per cent. lysol.

Statistics.—During the South African War, when prophylactic inoculation was incompletely practised, there were 60,000 cases of enteric, with 8,227 deaths. The complete figures for the Great War are not yet to hand, but it is known that, although millions of men were under arms, for the first two years of the War only some 4,000 cases of enteric were reported from France, with a case-mortality of less than 2 per cent. In the Navy, Bassett Smith's statistics record an incidence of only 144 cases of enteric during the year 1917, of which 8 occurred in inoculated and 66 in uninoculated individuals.

The American Army shows much the same figures; for two years, 1917-19, out of an average strength of over two million men, there were only 213 deaths from enteric, and it is calculated that had typhoid prevailed in the same proportion as in the uninoculated troops in the Spanish-American War the death-roll from this cause would have been over 60,000.

Measures to avoid infection.—The most certain method of avoiding enteric infection is the water-carriage system of sewage disposal. This, however, is not general in the tropics, so that other methods must be considered. These are: (*a*) detection of enteric carriers and their control, especially in relation to the manufacture, distribution, and cooking of food; (*b*) protection of water supplies; (*c*) extermination of flies, and preventing them from access to

Digitized by Google

excreta and refuse on the one hand, and to food for human consumption on the other.

Treatment.—There is no specific therapy (vaccine or serum) of proved value for enteric fever; nor is there any drug which is known to exercise an active influence over this disease. In these circumstances it is best to confine treatment to providing the best hygienic conditions, good nursing, and careful dieting. All that the great majority of mild paratyphoid cases require is a soap-and-water enema every other day to relieve the constipation. Milk should be the diet while the patient is febrile; thereafter custard, milk pudding, soup, fish, and meat diet. The diet should contain about 70 grm. of protein a day, with a calorie value of 2,500–3,000. Water should be given freely. Purgative medicines should be avoided. The care and cleanliness of the mouth and teeth are important. In cases of great toxicity with high temperature (over 102·5° F.) and no morning remissions, tepid sponging is useful; in the worst cases the cold bath or ice pack may be resorted to. The temperature of the water should be between 70° and 85° F.; a tub of canvas and mackintosh sheeting may be improvised. Food may be given as a stimulant after the bath. The rectal temperature should be taken immediately on removal from the water, and again three-quarters of an hour later. Of late, *vaccine-therapy* has been employed; the homologous organism should be given, subcutaneously or intravenously, in small doses, 25–50 millions on each occasion. The injection may be repeated every third day.

The management of convalescence calls for special care, especially in paratyphoid-A infections, and a return to solid diet should be postponed until the temperature has been normal for at least ten days.

For the bacilluria associated with enteric, urotropine (hexamine) in doses of 10 gr. three times a day acts as a specific.

"Typho-Malarial Fever"

Some years ago a good deal was said, particularly in America, about "typho-malarial fever." An idea got abroad that there is a specific disease which, though resembling both, is neither typhoid nor malarial, nor any of the other recognized forms of continued fever. It is, in fact, ordinary enteric in a person infected with the malaria parasite.

It has already been pointed out that the malaria germ may remain dormant for months or even years in the body, and then, on the occurrence of severe physiological strain—such as a chill, shock, excessive fatigue, and so forth—wake up again, and once more

Digitized by Google

multiply and flourish in the blood and give rise to the phenomena of malarial fever. It is a recognized clinical fact—one familiar to our predecessors and much insisted on by them—that any disease process occurring in a person who has once had malarial fever is prone to take on an intermittent or periodic character, as if the previous malarial infection had left a sort of impress of periodicity on the constitution. And so it comes to pass that an attack of typhoid in malarial countries, or in persons returned from malarial countries, is prone to assume some of the characters of intermittent or remittent fever.

Not infrequently, instead of the slowly increasing headache, malaise, creeping cold, anorexia, and day-by-day ladder-like rise of temperature, the first recognized sign of typhoid in such circumstances is a violent rigor, immediately followed by rapid rise of temperature, which in an hour or two mounts to 104° or 105° F., to be succeeded in a few hours by profuse sweating and a partial remission of fever exactly resembling an attack of ague. For the next two or three days these attacks are repeated, the remissions becoming less complete each time. Quinine may be given; but although the rigors and marked oscillations of temperature are checked, the practitioner is surprised and disappointed to find that the temperature keeps permanently too high, and that the typhoid state is gradually developed. Or it may be that a typhoid fever begins in the usual insidious way, runs its usual course for a week or two, and then, in the middle of what is regarded as an ordinary typhoid, rigors and temperature oscillations and other malarial manifestations occur. If quinine is administered these oscillations cease and the typhoid resumes its usual course. Or it may be that it is not until the end of the fever and during convalescence that these malarial symptoms are developed. Several such cases are now on record in which the malaria parasite was found in the blood.

The **diagnosis** between typhoid and some forms of malarial remittent is often exceedingly difficult, in certain cases almost impossible without the assistance of the microscope and the serum test. The principal points to be kept in view are: First, the mode of incidence of the disease. In typhoid there is a gradual rise of temperature, a daily gain of a degree or so during several days, the maximum not being attained for five or six days; as against the sharp rigor and sudden rise of temperature through five or six degrees in the first few hours in malarial fever. Secondly, the characters of the gastric symptoms differ. Thus, in malarial remittent there are bilious vomiting and perhaps bilious diarrhœa,

Digitized by Google

tenderness of the liver, epigastrium, and spleen, and an icteric tint of skin and scleræ; in contrast to the abdominal distension, perhaps the iliac tenderness and gurgling, and the peasoup stools of typhoid. Such signs as epistaxis, deafness, and cheek-flushing in typhoid have a certain weight, but skin eruptions in the tropics are of little aid in the diagnosis of such cases. Prickly heat, or its remains, is present in nearly everyone, sick and healthy, malarial and typhoid patient alike; so that rose spots are to be found in nearly all fevers in hot weather. None of these signs can be considered as absolutely diagnostic; all or any of them may be present in typhoid, and all or any of them may be present in malarial remittent. The only really diagnostic marks are tertian or quartan periodicity, amenability to quinine, and, above all, that supplied by the malaria parasite in the blood and the Widal serum test. In all doubtful cases the malaria parasite should be sought for; if it is found, the case has certainly a malarial element, and quinine is indicated. If it is not found, and if quinine has not been administered and several negative examinations of the blood have been made, the case is probably one of pure typhoid. Nevertheless, if the malaria parasite is found, typhoid is not necessarily excluded.

No one who is proceeding to the tropics to practise medicine should fail to familiarize himself with the technique for the Widal reaction (p. 897). In Europe he can fall back on the bacteriologist; in the tropics, as a rule, he cannot do this.

Enteric-like Fevers

Bacillus fæcalis alkaligenes septicæmia.—During recent years, especially during the War, a series of mild pyrexias, of either remittent or intermittent type, has been proved by Hirst and others to be due to infection with this organism. (Table, p. 408.) It is a common inhabitant of the intestinal canal, where it is not known definitely to exert any pathogenic action. The fever it gives rise to when present in the bloodstream may last from two to fifteen days. It shows an evening rise with marked morning remission. (Chart 22.) The symptoms resemble those of a mild enteric, the pulse is slow in relation to the temperature, and the tongue is slightly furred. In some cases the patient's serum clumps the homologous organism in a dilution of 1 in 50. In outbreaks of food-poisoning or "ptomaine poisoning," which occur from time to time, bacilli of the Salmonella group, *B. enteritidis* and *B. aertrycke* (*suipestifer*), have been isolated from the bloodstream. The fevers they produce have many features in common

Digitized by Google

with enteric. They differ in the suddenness of the onset with rigors, the accentuation of the gastro-intestinal symptoms, the short duration and rapid termination of the fever. *B. aertrycke* resembles *B. paratyphosus-B* in its biochemical, but may be differentiated from it upon its serological reactions.

B. coli infections.—Infection of the bladder and urinary tract by *B. coli* is frequently met with in both sexes in the tropics. Should the organism enter the bloodstream it may give rise to a prolonged intermittent pyrexia resembling enteric. *B. coli* septicæmia and pyæmia may be a terminal infection in debilitated natives, especially after bacillary dysentery; in these cases the organisms gain

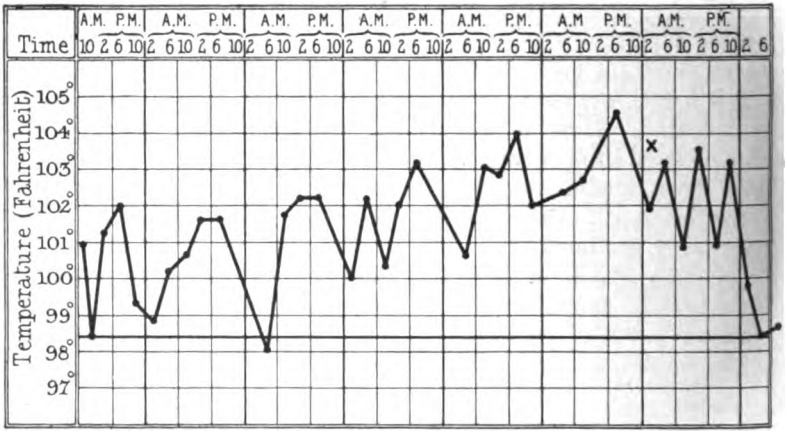


Chart 22.—B. fæcalis alkaligenes septicæmia. (*Bellingham-Smith.*)
× Bacillus isolated from blood.

entrance to the bloodstream through the intestinal lesions, and, becoming arrested in the glomeruli, give rise to multiple minute abscesses in the cortex of the kidneys, from which they escape in an intermittent manner and appear in the urine. (Fig. 81.) The condition is probably much more widespread than has been recognized hitherto. A series of cases from Egypt has been described by Enright and the Editor. The general condition of the patient, the stupor and the intoxication, may resemble those of enteric, but the onset is generally sudden, with headache, and acute pain referred to both kidney regions. Usually all symptoms of vesical irritation are absent. The tongue is thickly furred; rigors are numerous and accompanied by profuse sweats. The organism may be recovered in pure culture from the bloodstream during

Digitized by Google

the rigors, as well as from the urine by ureteric catheterization. The acute attacks are liable to be confused with those of malaria. (Chart 23.) The only form of treatment of any avail would appear to be intravenous injection of 40 c.c. of freshly prepared eusol.

Fig. 81.—Bacillus coli septicæmia. (*Orig.*)

1, Aggregation of organisms in intertubular capillaries; 2, large collection of organisms in a medullary vein; 3, passage of bacilli through tubular epithelium of duct of Bellini into lumen.

To make eusol solution.—Eusol, to be effective, must be made up freshly just previously to injection. The following method is recommended: 12·5 grm. of chloride of lime (bleaching powder) and 12·5 grm. of boric acid are intimately mixed and added to 1,000 c.c. of distilled water. After standing overnight the mixture is filtered, and the filtrate, termed *eusol*, will be found to contain approximately—

Hypochlorous acid	0·26 per cent.
Calcium biborate	1·28 „
Calcium chloride	0·17 „

Digitized by Google

The amount of hypochlorous acid can be estimated by titration against a decinormal solution of sodium arsenite, using a solution of potassium iodide and starch as an indicator. For intravenous use, 8·5 grm. of sodium chloride are added to each litre of eusol, and the injection given at 37° C.

Imperfectly Differentiated Fevers of the Tropics

There can be little doubt that, in addition to those already mentioned, there are several fevers in the tropics whose etiology is as yet insufficiently understood, and it is possible that future research may reveal a still greater number of organisms which are capable of causing a bacillæmia. These may be included among the puzzling pyrexias which in military practice are included under the heading of "Pyrexia of unknown origin." Formerly Crombie divided these fevers on clinical grounds into *simple continued fever* and *non-malarial remittents*, and Manson described a *double continued fever* in China. Recent research has shown that a considerable proportion of these may be classified as paratyphoid fever or some allied form.

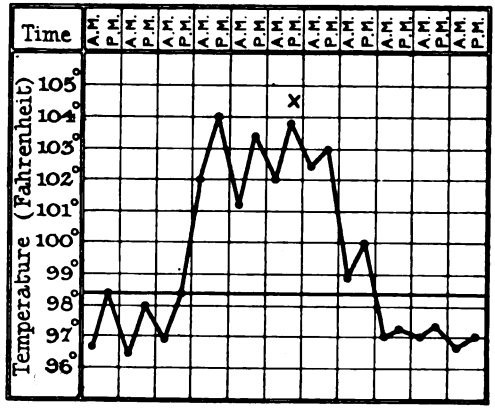


Chart 23.—B. coli septicæmia. (*Enright and Manson.*)
× *B. coli* isolated from the blood.

Low fever.—This type of fever is not an unusual one among Europeans in the tropics. Its characteristics are indefinite duration—weeks or months; a persistent though slight rise of temperature, rarely above 101·5° F. but never below 99°; anorexia, debility, loss of flesh, and a tendency to bilious diarrhœa. It is unrelieved by quinine or arsenic; but it almost invariably responds to a change of air, especially to a trip at sea.

Unidentified fever of Cairo.—There still remains to be mentioned a peculiar prolonged *remittent pyrexia*, lasting three weeks on an average, which was noted in Cairo in the early months of 1915. In all there were over 1,500 cases, with a case-mortality rate of 22·38 per cent. In many of its clinical manifestations the disease

Digitized by Google

resembled typhoid or paratyphoid fever, though it gave none of the laboratory tests of those diseases. Various forms of exanthematous rashes were noted towards the close of the first week in a third of the cases, and a roseolar rash covered the whole body. The onset of the pyrexia was insidious, it terminated most usually by lysis, and was specially prone to relapse. Pulmonary and bronchial complications were commonly met with, as were also parotitis and gangrene of the extremities.

Digitized by Google

CHAPTER XXII

HEAT-STROKE

THE term "heat-stroke" conveys the suggestion that heat is the leading etiological factor in the various morbid conditions which custom has grouped under this and similar names.

The expression covers several distinct, one might say of two of them almost opposite, clinical conditions. One of these is *heat-exhaustion*, virtually a syncope, which may occur anywhere and in any climate, high atmospheric temperature, whether natural or artificial, being its essential etiological factor. The other, of which hyperpyrexia is the most striking clinical feature, is a well-defined fever, having a peculiar endemicity and assuming at times in the endemic area almost epidemic characters.

Besides these two well-defined morbid states associated with high atmospheric temperatures there is another but ill-defined group of heat-stroke cases which, to all appearance, result exclusively from exposure to the direct rays of the sun. These cases might be classified under the term *sun-traumatism*.

Although not all of them are strictly classifiable as fevers, in deference to custom and for convenience these three phases of so-called "heat-stroke" will be described in this place and as a group.

HEAT-EXHAUSTION

Definition.—Sudden faintness, or fainting, brought about by exposure to high atmospheric temperature.

Etiology.—The healthy human body, when untrammelled by unsuitable clothing, when not exhausted by fatigue or excesses, when not clogged by surfeit of food, by alcoholic drinks or by drugs, can support with impunity very high atmospheric temperatures. In many parts of the world men live and work out of doors in temperatures of 100° or even of 120° F. Many industries are carried on at temperatures far above this—glass-blowing, sugar-boiling, for example. The stokers of steamers, especially in the tropics, discharge for hours their arduous duties in a temperature often over 150° F.

When, however, the physiological activities have become impaired by disease, especially by heart disease, kidney, liver, or

Digitized by Google

brain disease, by malaria, by alcoholic or other excesses, by fatigue, by living in overcrowded rooms; or when the body is oppressed by unsuitable clothing; or in the presence of a combination of some of these—then high atmospheric temperatures are badly supported, the innervation of the heart may fail, and syncope may ensue.

Heat-exhaustion, then, is one form of what, when the subject of it happens at the time to be exposed to the sun, is called "sun-stroke," or when the patient happens to be at the time under cover is called "heat-stroke."

Symptoms.—When attacked with heat-exhaustion the patient feels giddy, and perhaps staggers and falls. He is pale; his pulse is small, soft, and perhaps fluttering; his breathing is shallow, perhaps sighing, never stertorous; his pupils are dilated; his skin is cold; his temperature is subnormal; and he may be partially, more rarely wholly, unconscious. Usually after a short time he gradually recovers; very likely with a splitting headache and feelings of prostration. In a small proportion of cases the faint is not recovered from, and death ensues.

Treatment.—In syncopal heat-stroke the patient should be laid at once on his back in a cool, airy, and shaded place. His clothes should be loosened, a little water dashed on his face and chest, and ammonia held to his nostrils. If necessary, a stimulant may be given by the mouth, or injected into the rectum or hypodermically. It is a mistake to douche these cases too freely. The object is rather to stimulate than to depress.

Heat-Hyperpyrexia

Definition.—An acute disease developing in the presence of high atmospheric temperature, and characterized by sudden incidence of hyperpyrexia, coma, and extreme pulmonary congestion and œdema.

Nomenclature.—This is, perhaps, the most important of the several diseases covered by those loosely used terms—sun-stroke, heat-stroke, *coup de soleil*, insolation, heat-apoplexy, heat-asphyxia, thermic fever, etc.—but is best known as heat-hyperpyrexia.

The **geographical distribution** of heat-hyperpyrexia appears to be remarkably restricted. Although it is certain that this type, or what passes for this type, of disease has been reported as occurring in many countries, on making careful examination it will be found that a large proportion of the reputed cases are really samples of other diseases, more especially of cerebro-spinal fever, apoplexy, tuberculous meningitis, delirium tremens, pernicious malaria, or some other phase of acute disease, but not of true heat-hyperpyrexia.

Digitized by Google

It is unknown in Europe. The endemic areas are—in America, the east coast littoral of the United States, more especially in the great towns, the Mississippi valley, the coast of the Gulf of Mexico, the valleys of the Amazon and of the La Plata, and the South Atlantic coast; in Africa, the valley of the Nile, the coasts of the Red Sea, and a low-lying part of Algeria near Biskra; in Asia, Syria, Mesopotamia, the valleys of the Indus and Ganges, Lower Burma, Tonquin, and south-east China; in Australia, the Murray River district, the Queensland coast, and, possibly, the plains of Sydney. It is not met with on the high seas, although it is well known on ships in the narrow, land-locked Red Sea and the Persian Gulf. During the War dangerous cases occurred most numerously in Mesopotamia, especially during July, 1917, when for three days the temperature reached 122° F. in the shade, and 135° F. in the interior of double fly-tents. Heat-hyperpyrexia was not common in East Africa, nor in any other theatre of war.

Etiology.—New-comers to the endemic areas and Europeans are more liable than natives or residents of long standing. Men over forty are more susceptible than are those of younger age. Apparently, long residence confers a relative although not an absolute immunity.

All ages and both sexes are susceptible; but in consequence of their habits and more frequent exposure to the predisposing and immediate causes, men are more subject to heat-hyperpyrexia than are women.

Influences similar to those predisposing to heat-syncope and sun-traumatism predispose to heat-hyperpyrexia. Among these are all physiological depressants—notably intemperance, fatigue, overcrowding, unsuitable clothing, malaria, acute disease, constipation, and also chronic organic diseases of the important viscera.

Heat-hyperpyrexia has generally been attributed to direct action of atmospheric or solar heat on the body. Many theories of the *modus operandi* of this assumed cause have been advanced. Among these may be mentioned superheating of the blood by the high temperature of the surrounding atmosphere; paralysis of the thermic centres causing (*a*) over-production of heat or (*b*) retention of body-heat; pressure on the brain by expansion from heating of the cerebro-spinal fluid; vaso-motor paresis; paresis of the heart ganglia; excess of carbonic acid in the blood; coagulation of myosin; suppression of sweat; deficient serosity of the blood from excessive sweating, and so forth.

Most authorities agree that a process of auto-intoxication occurs,

Digitized by Google

as evidenced by indicanuria. Acetone and diacetic acid occur in the urine of 12 per cent. of cases, but the idea of a generalized acidosis is not accepted. Hearne has pointed out that heat-hyperpyrexia is associated with suppression of sweat, which may occur forty-eight hours before the attack. With sweating suppressed, the body-temperature tends to adjust itself to that of the atmosphere, but, in view of the increased respiratory and nitrogenous changes, is unable to do so when it reaches 108° F., at which point coma, delirium, and convulsions appear. The possibility of this theory being correct is shown by the liability to heat-hyperpyrexia after hypodermic injection of atropine. Similar results have been produced in lower animals by Cramer, by injection of β-tetra-hydronaphthylamine, which over-stimulates the thyroid-adrenal apparatus. After prolonged exposure to high temperatures the sweat apparatus becomes exhausted and the glands naturally cease to function.

Symptoms.—Though sometimes coming on suddenly during exposure to the sun, heat-hyperpyrexia is very often preceded by a distinct prodromal stage. It is frequently developed independently of any direct exposure to the sun; not seldom the attack comes on during the night.

Among prodromata, which may show themselves with greater or less distinctness for an hour or two or even for a day or two before the full development of the attack, may be mentioned great disinclination for exertion, pains in the limbs, drowsiness, vertigo, headache, mental confusion, sighing, anorexia, thirst, intolerance of light—sometimes accompanied by chromatic aberrations of vision, suffused eyes, nausea and perhaps vomiting, præcordial anxiety, sometimes a sense of impending calamity, an hysterical tendency to weep, a very hot dry skin, and a quickened pulse. Longmore, Willcox, and others have called attention to excessive irritability of the bladder as a common prodromal symptom. This is a valuable and easily-recognized danger-signal. The latter observer has drawn attention to the loss of knee-jerks which occurs; their return may be regarded as of favourable prognosis.

Though generally present in greater or less degree, and for a longer or shorter time, in many instances these prodromal symptoms are not remarked, the first indication of anything wrong being perhaps a short stage of restlessness, or possibly of wild delirium. This brief preliminary stage rapidly culminates in coma, complete unconsciousness, and high fever, quickly passing into hyperpyrexia which may reach 110° F.

Digitized by Google

The pupils, unless immediately before death, when along with the other sphincters they relax, are contracted. The reflexes are partially or wholly in abeyance. There may also be, especially in the graver cases, free watery purging, the dejecta as well as the skin of the patient emitting a peculiar and distinctive mousy odour. The scanty urine may contain blood-corpuscles, albumen, and casts.

Willcox distinguishes different clinical types of heat hyperpyrexia :

(1) *Gastric type.*—A most deceptive form, in which the axillary temperature is normal, the rectal temperature raised, and gastric symptoms predominate, with congestion of the liver. A fatal hyperpyrexia may develop without previous warning.

(2) *Choleraic type.*—This form is of sudden onset, with purging and general resemblance to true cholera ; it may be fatal within three or four days. The rectal temperature may rise to 110° F. after death.

(3) The *true heat-hyperpyrexia*, in which nervous symptoms predominate, has already been described. It accounts for 70 per cent. of the cases.

Unless active measures to lower temperature are taken early in the progress of the case, and these measures are vigorously carried out, in the great majority of instances death will occur within a few hours, or even minutes, of the onset of insensibility. The immediate cause of death is generally the failure of respiration. Rarely do cases linger for a day or two. Partial recovery is sometimes followed by relapse. In favourable cases the disease usually terminates by crisis. Convalescence is rapid. Unless the patient is moved into different surroundings a relapse may occur ; two or even three have been recorded. Occasionally cerebral or cerebellar symptoms may persist.

Mortality.—As might be supposed, some types of heat-stroke are much more dangerous than others ; heat-hyperpyrexia infinitely more so than ordinary heat-exhaustion. Treatment, if early instituted and judiciously carried out, has undoubtedly a powerful influence in reducing mortality. Taking one type of heat-stroke with another, the case-mortality among British troops in Mesopotamia was about 8 per cent.

Morbid anatomy.—A notable feature in fatal hyperpyrexia is the early appearance of rigor mortis. The blood is remarkably fluid, or but feebly clotted. The venous system is loaded, dark fluid blood pouring from the phenomenally engorged lungs and other viscera on section. Both blood and muscles are said to yield an

Digitized by Google

acid reaction more or less pronounced. It has been stated that the red blood-corpuscles are crenated and do not form rouleaux. If the post-mortem examination is made shortly after death and before decomposition changes have set in, the heart in early rigor mortis, particularly the left ventricle, will be found remarkably rigid; this rigidity is sometimes described as being of woodeny hardness. There may be some venous congestion of the meninges, but the brain itself shows no important vascular or naked-eye changes. On microscopic examination, necrotic changes in the ganglion cells with chromatolysis of the nuclei are found. The cerebro-spinal fluid is clear and under pressure. Cortical changes in the suprarenals have been described. The intestinal mucosa, as well as that of the stomach, is swollen and exhibits patches of congestion. The temperature of the cadaver continues to rise after death, and may reach 114° F.

Diagnosis.—The presence of high fever is sufficient to differentiate heat-hyperpyrexia from sudden insensibility caused by uræmia, by diabetic coma, by alcoholic and opium poisoning, and by all similar toxic conditions. Cerebral hæmorrhage, particularly pontine, may, after some hours, be followed by high temperature; but here the febrile condition follows the insensibility, whereas in heat-stroke the febrile condition precedes insensibility. The diagnosis from a cerebral malarial attack may be very difficult; chief reliance has to be placed on the history if obtainable, on the condition of the spleen, and especially on the result of microscopical examination of the blood. Malarial fevers, and the early stages of the eruptive fevers in children, are very apt to be regarded as heat-stroke, particularly if there has been recent exposure to a hot sun. Cerebro-spinal fever, so often mistaken for heat-hyperpyrexia, may be recognized by the occipital retraction, the irregular pupils, the frequent occurrence of strabismus, Kernig's sign, the comparatively low and fluctuating temperature, the associated herpes, the initial rigor, and its duration.

Treatment.—In all fulminating fevers, including heat-hyperpyrexia, occurring in warm climates, if malaria be suspected, particularly if the parasite be discovered in the blood, quinine should be injected intravenously or intramuscularly at once (7–10 gr. of the bihydrochloride), or given by enema as directed under Malaria (p. 72); this dose should be repeated three or four times at intervals of four hours. In every case of heat-stroke, whether it has been deemed advisable to administer quinine or not, attempts must at once be made to reduce temperature by such rapidly acting measures as the cold bath, or ice applied in various ways to the

Digitized by Google

head and body. Antipyretic drugs are of very little service, even if, in consequence of their depressing action on the heart, they be not actually dangerous; in all serious cases of heat-stroke such drugs must be carefully avoided. The patient should be placed on a wet sheet supported upon bed cradles, thus forming a moist chamber in which he lies; the whole may rest upon a rush-covered bed or *angareeb*. With the aid of a fan a sufficiently cool atmosphere is produced. The continuous water-spray with iced water, together with an electric fan, simulates the natural process of sweating to the best advantage. Rubbing the skin with ice, by constricting the capillaries, apparently only obstructs evaporation. Mackintosh sheets should be avoided, as they become grossly overheated and rapidly convert the stream of cool water into a hot bath. A thermometer is kept in the rectum. The application of cold should be at once discontinued so soon as the thermometer in the rectum has sunk to 104° F., or, in cases of simple thermic fever in which the temperature has not exceeded 106°, when it has fallen to 102°. If these powerful antipyretic measures are carried beyond this point the fall of temperature may continue below the normal, even to as low as 91°, and dangerous collapse ensue.

On discontinuance of the iced sheet the patient should be wrapped in a dry blanket. Very likely perspiration, a favourable sign, will then set in. Stimulants may now be necessary. Strychnine, owing to the marked tendency to convulsions incidental to heat-stroke, must on no account be used as a cardiac stimulant. Convulsions are best controlled by cautious venesection. As death in heat-stroke generally results from failure of respiration, Hearne and others strongly recommend artificial respiration when the breathing threatens to become suspended; they claim to have obtained some marvellous results from this expedient. It should be kept up for half an hour or longer. Chloral enemata are useful in delirious cases. With a view of relieving intracranial pressure Rawling has performed decompression with success; at any rate, lumbar puncture is indicated in cerebral cases as being a rational method of relieving the pressure. Intravenous or subcutaneous injections of saline are indicated in the choleraic forms. According to Willcox the gastric cases should receive a liberal supply of bicarbonate of soda—30 gr. every two hours.

During convalescence great care must be exercised to shield the patient from all influences calculated to provoke relapse. The power of sweating may be in abeyance for three weeks or longer.

Digitized by Google

Sun-Traumatism

There is a large group of heat-stroke cases ill-defined, and difficult to classify, which belong neither to the category of heat-exhaustion nor to the very definite condition just described. The morbid phenomena in this type of sun-induced disease are attributable, apparently, to a peculiar physical action of the direct rays of the sun on the tissues. To this category belong, it seems, those sudden deaths occurring without warning during, and manifestly in consequence of, exposure to the sun. Such may have been the sudden deaths, described by Parkes, Maclean, Fayrer, and others, in which soldiers in the excitement and stress of battle, while oppressed with thick clothing and heavy accoutrements and exposed to a blazing sun, suddenly fell forward on their faces and, after a few convulsive gasps, died. In these instantaneously fatal cases the paralysis of the heart or respiration seems to be of the nature of shock, as from a blow or other sudden and violent injury to the encephalon.

Doubtless, indeed it is a well-known fact, the strain undergone in these and similar circumstances may, in some instances, cause an apoplexy or rupture of some description in tissues prepared for such a cataclysm by morbid degenerations of long standing.

Besides the foregoing there is another type of case in which, after prolonged exposure to the sun, a febrile condition is established. This is sometimes of great severity, being characterized by intense headache, a rapid full pulse, a pungent dry skin, intolerance of light, sound, and movement, and occasionally by vomiting or delirium. This condition suggests meningeal congestion, possibly inflammation. The acute phase may be quickly recovered from, or it may prove very persistent and last for days or weeks. It may leave no injurious effects; or it may be followed by a variety of transient or more permanent morbid nervous phenomena. Among the sequelæ authors have mentioned tremor, loss of memory, amaurosis, deafness, various paretic conditions, epilepsy, insanity, persistent headache, recurring headache, and dyspeptic conditions. How far these sequelæ are entirely attributable to sun-exposure, or how far they depend on other diseases, as syphilis for example, the local cerebral manifestations of which may have been provoked, though not actually caused, by the sun-traumatism, it is not always easy to say.

The **morbid anatomy**, as well as the clinical symptoms, indicates meningitis as a feature of these instances of reputed sun-traumatism. Authors refer to thickenings and opacities of

Digitized by Google

the meninges, and even to thickening and roughening of the calvarium.

Many speculations have been advanced as to the **pathogenesis.** Manifestly it is not altogether, if at all, a question of caloric, for such effects do not result from exposure to the heat of a furnace, however intense. There appears to be some special element in the solar rays capable of injuriously affecting the tissues, particularly if they have not become gradually habituated to sun-exposure. That some such element does exist is proved by the phenomena of sun-erythema, of that form of skin pigmentation known as sun-burning, and, possibly, of leucodermia. The sensation of distress brought on by exposure to a hot sun, which is quite a different sensation from that produced by the heat of a fire, points in the same direction. In this connection we are forcibly reminded of the phenomena of the actinic rays of the solar spectrum, and of the remarkable tissue changes induced by the Röntgen rays.

Treatment.—Patients suffering from sun-traumatism must be kept as quiet as possible in a cool, airy, and darkened room. For a time the head should be kept shaved, and cold applied to the scalp. The bowels must be free; food should be light and unstimulating, and alcohol in every form strictly forbidden. Restlessness and insomnia are best treated by the bromides. For a considerable time the patient will be troubled with loss of memory, and feebleness of intellectual power and of the faculty of concentration. He may be irritable, liable to headache, and extremely sensitive to heat—more particularly the heat and glare of the sun. So soon as he is able to be removed he must be sent to a cooler climate, and there remain until all trace of his illness has completely disappeared. Indeed, it is questionable if the subject of pronounced sun-traumatism should ever again risk the dangers of a tropical climate; certain it is that he should not return to the tropics so long as the slightest evidence of cerebral trouble remains.

For persistent headache and other signs of chronic meningitis, courses of the iodides and bromides, repeated blistering of the neck and scalp, together with careful dieting and general hygiene, should be tried. In not a few instances, in spite of the most careful treatment, medicinal and climatic, serious permanent disease of the encephalon remains, giving rise to various and often incurable troubles; very commonly, to distressing intellectual enfeeblement.

Prevention of Heat-Stroke

In heat-stroke climates great attention should be paid to the general health; if this be not satisfactory, exposure to the sun and

Digitized by Google

to high temperatures must, so far as possible, be avoided. Alcoholic drinks, gluttony, excess of animal food, too much tobacco-smoking —in fact, dissipation of all sorts—are especially to be deprecated. Individuals suffering from malarial or other fevers, or from chronic liver or kidney disease, run great risk if they are careless about exposing themselves to the sun. Violent exercise, excessive fatigue, want of sleep, constipation, are also to be avoided.

Clothing ought to be light and loosely fitting, the under-garment being of thin woollen material. In going out in the sun the head must be protected by a wide-brimmed, well-ventilated pith hat shielding the temples and neck as well as the top of the head. An actinic theory of sun-traumatism, advocated many years ago by Maude and Duncan, and more recently by Sambon, indicated the wearing of actinic-proof colours—red or yellow—closely interwoven in tropical clothing, though experiments conducted in the Philippines at the Institute of Science would seem to have disposed of the practical value of this theory. A pad of cotton sewn in the back of the coat in such a way as to protect the spine is a wise measure, and one adopted by experienced sportsmen in India. Puntone, who has shown by an ingenious experiment that the human cranium is diathermal to the yellow-red and ultra-violet rays, but absorbs the red and blue-green rays, recommends green material covered with white cloth to protect important parts, more especially the head, neck, and spine. The phenomena connected with the Röntgen rays suggest the possibility that there may be solar rays other than the ordinary heat and actinic rays which, although they may be able to pass through organic materials, can nevertheless be arrested by metals. If this be true for the sun, as well as for the Röntgen rays, a useful addition to the sun-hat would be a thin plate of some light metal placed between the layers of pith constituting the basis of the ordinary sola topee. A sheet of tinfoil or other light metal would not perceptibly add to the weight of the headgear. Such sun-hats are now manufactured. A white umbrella, lined with green or orange, ought never to be despised. Tinted (smoke colour) goggles are probably a protection, as they certainly are a great comfort in mitigating solar glare.

Rooms should be kept dark during the day, and cooled by means of punkahs, thermantidotes, tatties, venetians, and other contrivances to promote a free current of air. In barracks and ships there must be no overcrowding. In very hot weather European soldiers should, if possible, sleep under punkahs. Military drills should be reduced to a minimum, and take place in the cool of the morning only, and after the soldier has had a cup of tea or coffee

Digitized by Google

and some light food. Marches should be short, interrupted by frequent halts, and be got through, if possible, in the early morning. While marching the men ought to be in open order, relieved of all unnecessary equipment, belts and clothing, and well supplied with water—at least 1–2 gallons a day—carried in a porous canvas bag (*chagul*). Camps should be pitched in cool and airy spots and under large spreading trees free from undergrowth. Double canvas, one layer of which should be orange-tinted, and grass or boughs or rush matting, laid on the wall of the tent, will do much to mitigate the temperature within.

The degree of stagnation of the air may be gauged with accuracy by means of Leonard Hill's katathermometer.

Patients in hospital are especially liable to develop heat-hyperpyrexia. The most valuable practical method is to attempt to forestall the advent of heat-stroke by periodically inspecting the patients to find out those with commencing suppression of sweat.

Digitized by Google

CHAPTER XXIII

THE DIAGNOSIS OF FEVERS IN THE TROPICS

For the successful diagnosis of fevers in the tropics the utmost collaboration of the clinician and pathologist is necessary. The clinician cannot afford to neglect the assistance of laboratory methods, any more than the pathologist can afford to neglect the evidence obtainable from the clinical appearances of the patient and the salient features of his temperature chart.

To begin with, one must sound a note of warning that, preceding the diagnosis of a tropical fever, the commoner causes of pyrexia in temperate countries must constantly be kept in mind. At the outset every case should be examined from this standpoint. The possibility of *pulmonary tuberculosis* as a cause of pyrexia must not be overlooked. One often sees an obvious phthisis disregarded or mistaken for malaria on the supposition that *any pyrexia in or from a tropical country is necessarily tropical in origin.* (Chart 24.) The same may be said of secondary and tertiary syphilis, malignant endocarditis, general suppurative conditions such as empyema, urethral fever, *B. coli* pyæmia, bacilluria, pyelitis, malignant disease, and especially liver abscess. Influenza, again, may occur in worldwide epidemics, and has always to be considered. Fever may also occur in association with the idiopathic anæmias, as for instance pernicious anæmia, spleno-medullary leucocythæmia, and lymphatic leukæmia. A posterior urethritis or prostatitis or ischio-rectal suppuration due to secondary infection with *B. coli* or other organisms may give rise to rigors almost identical with those of malarial origin, and this fact must always be borne in mind.

Malaria.—Much information may be obtained from a simple blood examination; in the first instance this must be directed, in a country in which malaria is endemic, as it is in most parts of the tropics, towards the discovery of the malaria parasite in every case of fever, always remembering that this parasite often exists as a mere complication, superimposed upon some other infection such as enteric, undulant, or relapsing fever.

It is advisable to examine the blood before quinine has been exhibited; this applies to all forms of malaria, the benign

Digitized by Google

tertian, subtertian, and quartan, but more especially to the first-named.

There is an idea prevalent that the parasite can only be found in the peripheral blood during the short periods immediately preceding and following the malarial rigor; it is true they are more abundant at these periods, though it is usually possible to find them in the apyrexial period, especially in the case of the subtertian parasite. In this species the youngest and the most mature forms, the ring and the crescent, are found usually in the peripheral blood, while the rest of the cycle takes place in the internal organs; therefore it is frequently possible to meet with cases presenting the typical clinical appearances (splenomegaly, etc.) without demonstrable parasites.

On account of the pernicious symptoms which subtertian malaria may exhibit, it is necessary to examine the blood at the

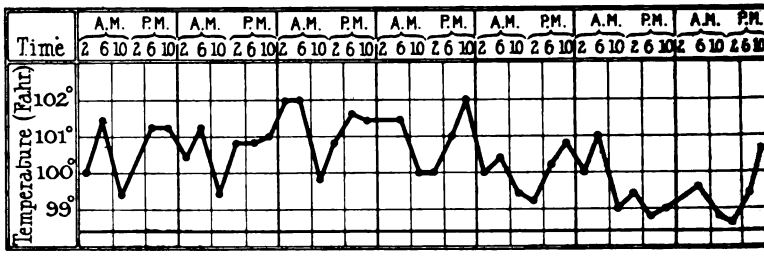


Chart 24.—Miliary tuberculosis. (*Dr. G. C. Low.*)

earliest possible moment. Even then one should remember that the parasites may only be found after a prolonged search, or, exceptionally, may even be absent entirely from the peripheral blood for thirty-six hours after the onset of fever.

Most usually, in the first attack of subtertian malaria, little assistance may be obtained from a study of the temperature chart, as this may closely simulate that of other fevers, especially enteric, though a double rise in the twenty-four hours is suggestive. (Chart 25.)

It may be taken as a general rule that in a malarious district a pyrexia, attended by a rigor during the forenoon or early afternoon, is almost invariably of malarial origin, and necessitates a blood examination for confirmation. Failing the discovery of the malaria parasite, a considerable rise in the mononuclears as ascertained by a differential count, the absence of any other ascertainable cause, amenability to quinine-therapy, indicate that the case is of malarial nature.

Digitized by Google

Relapsing fever.—Another parasite causing fever, and easily detected by simple blood examination, is the spirochæte of relapsing fever (p. 171). It is necessary to bear in mind, in order to confirm the suspicions aroused by the characteristic pyrexia, that these organisms are apt to disappear from, or become very scanty in, the bloodstream before the crisis. In other clinical forms, as for instance the relapsing fever of North Africa, Palestine, and Persia, they may be very scanty, so that a thick-film method may be required in order to demonstrate them microscopically. At the same time, even in the apparent absence of parasites, a considerable polymorphonuclear increase is suggestive of spirochætal disease.

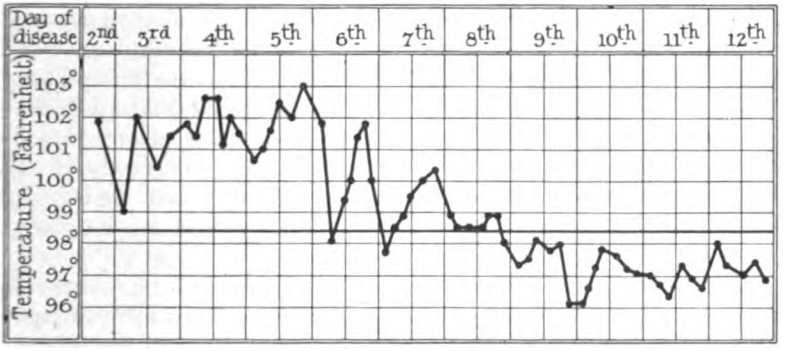


Chart 25.—Subtertian malaria simulating enteric. (*Orig.*)

Trypanosomiasis.—The diagnosis of trypanosomiasis need only be considered in the endemic zones of that disease and in travellers who have recently resided there. It mostly concerns the African, and to a lesser extent the Brazilian form (p. 138). The clinical symptoms—headache, glandular enlargement, and fugitive circinate erythema in the case of *T. gambiense* and *T. rhodesiense*, the enlargement of the thyroid in the case of *T. cruzi* with nocturnal pyrexia and headache—should suggest a prolonged search for the trypanosome. This must be done in a thicker film than is usually employed for malaria, and, as these protozoa are scanty in the peripheral circulation, search must be made with a $\frac{1}{6}$-in. lens, with which they may be easily detected. Failing the discovery of the parasite in the blood, gland and even lumbar puncture may be resorted to. Other suggestive points may be obtained from a persistent increase in the large mononuclear cells, together with a leucopenia and the presence of Kerandel's sign.

Digitized by Google

Kala-azar.—The diagnosis of kala-azar and its differentiation from chronic malaria is often a matter of considerable difficulty, as the two diseases may coexist. The clinical picture of splenomegaly with hepatic enlargement, a characteristic doubly remitting pyrexia with anæmia, a leucopenia and a mononuclear rise, should suggest hepatic or splenic puncture as a means of settling the diagnosis. Occasionally the Leishman-Donovan body may be found in the peripheral blood within the large mononuclear cells.

Yellow fever.—The recognition of yellow fever in its endemic haunts does not call for any special description, as it is made upon the general characters of the fever—the three-day incubation period, the icterus, the petechial hæmorrhages, black vomit, relative bradycardia, albuminuria, associated with leucopenia and a slight polymorphonuclear increase; but the attendant hæmolysis may cause great difficulty in differentiating it from the bilious remittent form of subtertian malaria, which may simulate it very closely, especially where yellow fever occurs sporadically, as in West Africa, and where possibly the two diseases may coexist in the same case. According to Noguchi, the *Leptospira icteroides* occurs but rarely in the bloodstream in sufficient numbers to be recognized under the microscope, and therefore too much reliance should not be placed upon its absence as a point in diagnosis.

Weil's disease.—The possibility of a pyrexia of otherwise unexplained origin being occasioned by the *Leptospira icterohæmorrhagiæ* must not be lost sight of by the practitioner in the tropics, and the differentiation of Weil's disease from yellow fever is a matter of considerable difficulty in countries in which the former disease occurs. Unlike *L. icteroides*, in a considerable number of cases *L. icterohæmorrhagiæ* may be demonstrated in a blood-film, though it is never abundant; it is more easily found in the urine. Therefore a polymorphonuclear leucocytosis along with grave icterus and splenomegaly should suggest examination of the urinary sediment for the leptospira, always remembering that this organism is not present in the urine till the twelfth day of the disease.

Seven-day fever.—A pyrexia remittent in type, with a tendency to relapse, together with a polymorphonuclear leucocytosis, should suggest the possibility of a fever being of spirochætal origin; the same is probably true of seven-day fever (p. 219), of which the saddle-backed type of temperature chart constitutes the most striking feature.

Dengue and phlebotomus fevers.—As regards the procedure in attempting a diagnosis in cases of pyrexia in which no parasites

Digitized by Google

can be demonstrated, one can obtain a great deal of information, if not a probable diagnosis, from a differential together with a total leucocyte count. A leucopenia with mononuclear increase and bradycardia is found in both dengue and phlebotomus fevers, and considerable difficulty may be experienced in differentiating these minor fevers from the graver ones already mentioned. Their respective endemic areas must be borne in mind; dengue, for instance, is common in the West Indies, the Pacific islands, and Australia, where sandfly fever is unknown or has not been recognized. Generally it occurs in a rapidly extending epidemic form. The joint- and bone-pains of dengue, the congested facies, the appearance of the rash on or about the fifth day of the attack in a considerable proportion of cases, the conjunctivitis in phlebotomus fever, though this is sometimes difficult to recognize, must be taken into account. These fevers, when in epidemic form, tend to occur at different seasons; the former is a disease of summer and early autumn, the latter of spring and the closing months of the year—that is, at the times when their insect intermediaries most abound.

Liver abscess.—In the absence of any specific parasite in the blood, a minute study of a four-hourly temperature chart is a most necessary adjunct, especially in long-continued remittent fevers. A continued pyrexia in which the fastigium occurs towards evening, together with a polymorphonuclear leucocytosis of 9,000 or over, associated with a peculiar pallor of the face, profuse sweats, and it may be with symptoms of involvement of the right lung, should make one suspicious of hepatic abscess, whether the *Entamœba histolytica* or its cysts are found in the fæces or not; generally a history of intestinal disturbance, not necessarily obvious, can be obtained.

Undulant fever.—A continued pyrexia with the fastigium of temperature in the early afternoon, together with a comparatively clean tongue, rheumatic-like joint-pains, and profuse sweats, should suggest the advisability of applying the Widal test for *melitensis* or *paramelitensis*. But the clinician should not expect a positive result early in the course of the disease.

Enteric.—A pyrexia with the fastigium in the late afternoon towards six o'clock, with the clinical appearances of enteric and, it may be, a roseolar rash and relatively slow pulse, should suggest a fever belonging to this group, but a clinical diagnosis must be confirmed whenever possible in the laboratory. The serum diagnosis in *uninoculated persons* is not a matter of grave difficulty, though the reaction does not appear until the end of the first week; in the case of paratyphoid-A, however, it may not appear until considerably

Digitized by Google

later, and this fact must not be lost sight of, and may explain many continued pyrexias of otherwise unexplained origin. A difficulty of considerable magnitude arises in *persons inoculated with a triple vaccine*. In these cases residual agglutinins to the respective organisms, typhoid, para-A and para-B, remain in the bloodstream for a year or more, and a serum diagnosis can only be made by employing frequent Widal tests and observing the rise in titre of agglutinins to one organism or the other (*see* Appendix III., p. 901).

Further confirmation of the specific cause of an enteric-like fever may be obtained by the isolation of the organism from the urine or fæces, but its late appearance in these excreta negatives its value for early diagnosis. In cases where no laboratory confirmation can be obtained, the atropine test should be employed.

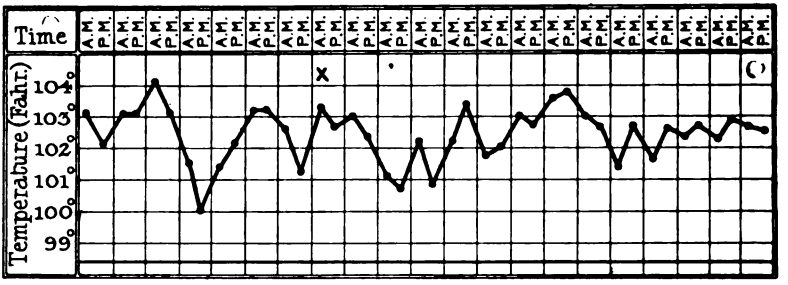


Chart 26.—Paratyphoid-B, four-hourly chart. (*After Garrow.*)
× Paratyphosus-B isolated from the blood.

Blood-culture still remains the most certain means of diagnosis in enterica and allied fevers, but a positive result can only be expected in about 30 per cent. of cases unless the blood is taken very early in the course of the disease. In confirming a diagnosis on clinical or serological grounds, the clinician should remember that the bacillus is absent from the bloodstream after the tenth day of the illness. (Chart 26.)

Fevers allied to enteric.—Blood-culture may also reveal organisms such as *B. fœcalis alkaligenes*, *B. aertrycke*, *B. gaertner*, and *B. suipestifer*, and the recently recognized *paratyphoid-C*, which are responsible for fevers in many ways resembling enteric clinically.

Typhus may be difficult to differentiate on clinical grounds from *relapsing fever*, and it should never be forgotten that the two diseases may coexist in the same patient. In the absence of positive laboratory assistance, typhus may be mistaken for *smallpox*, either

Digitized by Google

of the septicæmic or of the hæmorrhagic variety, early in the illness. In the differentiation attention should be paid to the characteristic backache of the latter disease, and the appearance on the third day of the hæmorrhagic rash affecting the inner aspect of the thighs, the forehead, and wrists in smallpox; while the bloated facies, the suffused eyes, delirium, mental stupor, foul breath and coated tongue, with hyperpyrexia persisting beyond the third day without the appearance of a rash, should suggest typhus. The subcuticular or petechial rash of typhus (so difficult to recognize on a dark skin) appears on the fifth or sixth day on the inner aspect of the thighs, the umbilicus, and the inner aspect of the arms, spreading to the remainder of the body and rarely involving the face. The serum-reaction of this disease (or the Weil-Felix reaction, Appendix III., p. 902) may be demonstrated after the fifth day of the illness. Cases of *enteric* with hyperpyrexia and psychological changes are rarely met early in the course of the disease. Their differentiation from typhus on clinical grounds may be a matter of considerable difficulty, and immediate resort should be made to blood-culture for *B. typhosus* (p. 895).

The seasonal incidence of tropical pyrexias may be of considerable assistance. Typhus is, as a rule, a disease of the cold or rainy season, when the native wraps himself up for the sake of warmth, and so encourages the propagation of the louse. For the same reason, *relapsing fever* is a disease of the early spring, to be followed at the commencement of the hot weather by *smallpox*, the spread of which is favoured by climatic conditions. *Malaria* of *benign* and *quartan* varieties is a disease of the hot season, while the *subtertian* variety occurs most frequently towards the autumn months. The seasonal proclivities of *sandfly-fever* and *dengue* have already been referred to.

Oroya fever as a tropical pyrexia need hardly be mentioned, as it has a very restricted distribution, and the fulminating character of the anæmia and blood-changes with which it is associated are found in no other tropical disease with which it could possibly be confused.

No mention has been made of *trench fever*, as its existence in the tropics and subtropics is as yet a matter of uncertainty.

Helminthic fevers.—An eosinophilia of 20–30 per cent. or over, with a leucocytosis, in a case of prolonged pyrexia should suggest a massive helminthic infestation. When this blood condition is associated with intense muscular pains, *trichinosis* may be considered and may be confirmed by microscopic examination of an excised piece of muscle. On the other hand, an eosinophilia

Digitized by Google

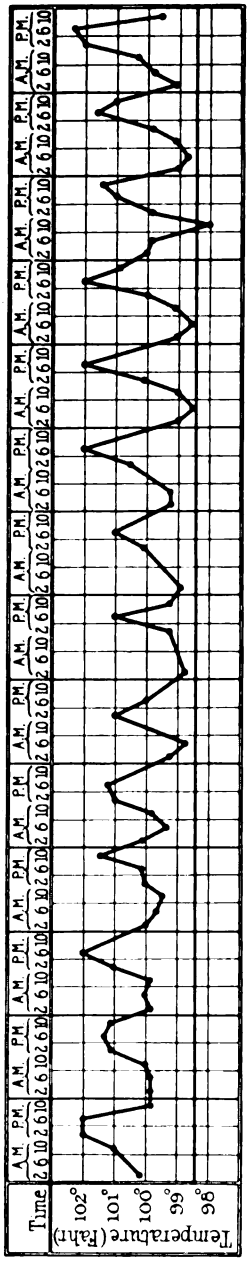


Chart 27.—Four-hourly temperature chart of acute schistosomiasis (S. mansoni). (*Lawton.*)

with a leucocytosis of 10,000–15,000 in a country where schistosomiasis (*Schistosoma hæmatobium*, *S. mansoni*, or *S. japonicum*) is endemic, in a patient with anæmia, emaciation, enlarged liver, tenderness over the gall-bladder, and a blotchy urticaria, should lead to a thorough and repeated search of the urine and fæces for the characteristic ova of these parasites. This urticarial fever is known in Japan as "katayama disease." (Chart 27.)

Filarial fever.—An eosinophilia of 15–20 per cent., with a moderate leucocytosis, in an endemic focus of filariasis, whether associated with visible lymphangitis or not, is strongly suggestive of filarial fever, even in the absence of the characteristic microfilariæ in the blood.

Hyperpyrexia (104° F. or over), in a patient who is stuporose and is severely ill, suggests, at first sight, several alternatives. It may be a case of subtertian malaria, relapsing fever, pneumonia, smallpox, typhus, typhoid, heat-stroke, or possibly plague. These are the alternatives that the tropical clinician has constantly to face. In the case of *subtertian malaria* and *relapsing fever* positive assistance may be obtained from a microscopic blood-examination early in the pyrexia, and *B. pestis* may occasionally be demonstrated in a blood-film in *plague septicæmia*. *Pneumonia* in the tropics is a much more pronounced septicæmia than in temperate countries, and the attention may not be attracted by any manifest respiratory embarrassment in the early stages; in these cases a physical examination of the lungs, combined with a polymorphonuclear leucocytosis and, very

Digitized by Google

occasionally, with demonstration of the pneumococcus in the bloodstream (Fig. 82), should focus attention on the lungs.

Rashes.—The differentiation of rashes in tropical pyrexias requires a brief mention. The polymorphous and almost indescribable rash of *typhus* has to be distinguished from the more florid exanthem of *dengue*, and it must be remembered that what would appear of roseate hue on a white skin may be brown, copper-coloured, or almost indistinguishable on a black one. The dengue rash has a diffuse reddish hue interspersed with areas of normal skin, while the typhus rash has a definite subcuticular appearance.

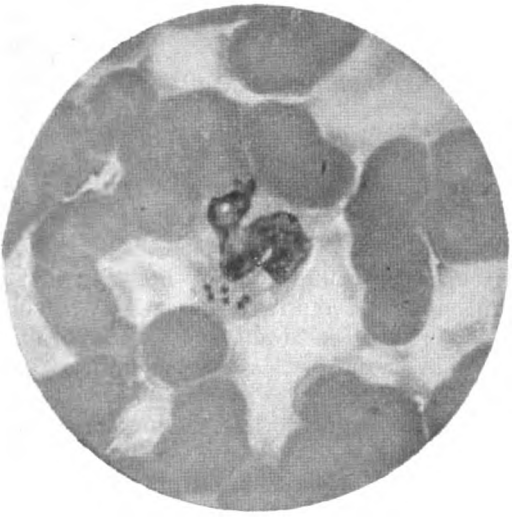


Fig. 82.—Pneumococci in leucocyte in peripheral blood. (*Original preparation.*) (*Microphoto: Dr. A. Norman.*)

Petechiæ or dusky mottling of the entire skin may occur in *cerebro-spinal fever*; in a dark skin it may be difficult to distinguish from typhus. Unless the former is very malignant in type, the meningeal involvement and the assistance obtained from lumbar puncture should make the distinction easy.

The papules of *smallpox* may be felt before they can be seen, especially on the forehead. Difficulty may be experienced in distinguishing the hæmorrhagic form from typhus in the early stages.

Scarlet fever, on the whole, is rare in most tropical countries, and is mild in the clinical phenomena it exhibits. The generalized erythema, occurring after an incubation period of two days, its

Digitized by Google

association with pharyngitis, a tendency to flaky desquamation, and a moderate leucocytosis assist in the diagnosis from *dengue*.

Measles has also to be taken into account; the appearance of the rash on the fourth day of the disease, its predilection for the face, the associated nasal and conjunctival catarrh, the presence of Koplik's spots on the buccal mucosa, are points which serve to differentiate it from *typhus* and *dengue*. The roseolar rash of *rubella*, the mildness of the general symptoms, and the lymphatic glandular enlargement make the diagnosis sufficiently obvious, so that German measles in the tropics presents no essential difficulty. Finally, the multiform erythematous rashes sometimes encountered in *enteric infections*, especially *paratyphoid-A*, must be mentioned. Their resemblance to certain types of typhus rash is marked; their appearance late in the fever, the absence of other clinical characteristics of the former disease, and the assistance of laboratory methods must all be considered.

Japanese river fever and *spotted fever of the Rocky Mountains* are characterized by rashes which greatly resemble typhus and appear about the same period in the course of the disease (fifth day). The rash of the former commences on the face; that of the latter on the forearms and legs, and may subsequently involve the whole body. As a factor in differential diagnosis they do not enter into account, except in those districts in which these two fevers are endemic.

Jaundice of hæmolytic origin is an important diagnostic feature in yellow fever, Weil's disease, blackwater fever, the bilious remittent form of subtertian malaria, and relapsing fever. The icterus of *yellow fever* is sufficiently characteristic, is often associated with petechiæ, and does not occur until the third or fourth day. The jaundice of *Weil's disease* also occurs about this time, with pruritus, irregular pyrexia, and suffusion of the conjunctivæ; it may be hardly recognizable, but there is usually a moderate splenomegaly. The intense jaundice of *blackwater fever* is dependent on, and appears simultaneously with, the hæmoglobinuria in severe cases. The yellow hue tends to deepen, and the diagnosis in this case is sufficiently obvious. The jaundice of *bilious remittent fever* (subtertian malaria) resembles that of yellow and blackwater fevers, but is generally of a deeper hue; it appears about the second day after the onset. The icterus associated with *relapsing fever* appears in severe cases during the pyrexial period immediately preceding the crisis, and is accompanied by great prostration and often by a painful enlargement of the spleen.

Digitized by Google

Obstructive jaundice may occur late in the course of hepatic abscess, but is rare.

Glandular enlargement in association with tropical fevers is met with most commonly in bubonic plague, trypanosomiasis, filariasis, climatic bubo, rat-bite fever, and kala-azar. The adenitis of *plague*, *rat-bite fever*, and *filariasis* is a painful one. In the former two the path of entry of the virus can usually be ascertained. In *filarial* adenitis the existence of other glandular enlargement and the accompanying lymphangitis are of considerable assistance in forming a diagnosis. In *trypanosomiasis* glandular enlargement confined to the posterior triangle of the neck is uniform, generally painless and discrete. Gland puncture will assist in diagnosis. In *kala-azar* the same group of glands may be involved, and on excision the parasite may be demonstrated; mere puncture as a rule is unsuccessful. The glandular involvement of *climatic bubo* is generally a subacute one and unassociated with severe systemic disturbance.

Diarrhœa is not usually a prominent symptom of tropical fevers. It may be noted, however, that a diarrhœa which may be hæmorrhagic is often associated with subtertian malaria, and may be present also in the enteric fevers and liver abscess.

Digitized by Google

Section II.—GENERAL DISEASES OF UNDETERMINED NATURE

CHAPTER XXIV

BERIBERI

Synonyms.—Kakke ; Barbiers ; Polyneuritis Endemica.

Definition.—Beriberi is a form of multiple peripheral neuritis occurring endemically, or as an epidemic, in most tropical and subtropical climates, and also, under certain conditions, in more temperate latitudes. The mortality is considerable, death usually depending on heart paresis.

Historical.—The special nature of beriberi was recognized by the Dutch in the early years of their intercourse with the East. Later, it was studied by British physicians in India, particularly by Malcomsen, Carter, Waring, and Morehead. It was not until a more recent epidemic in Brazil that beriberi began to receive attention from the present generation of medical men ; and only when Anderson, Simmons, Scheube, and Baelz took up the subject in Japan was it studied by modern methods, accurately defined, and its true pathology apprehended. Scheube and Baelz were the first to show distinctly that beriberi is of the nature of a peripheral neuritis similar to that of diphtheria and of alcohol—a view subsequently confirmed and adopted by Pekelharing and Winkler, and by most subsequent observers. More recently, and mainly owing to the investigations of Eijkman, Braddon, Cooper, Fraser, Stanton, Funk, Vedder, Hopkins, Hausette, Chick and Margaret Hume, its principal—it may not be the only—etiological factor has been shown to be a dietary of which the staple ingredient is overmilled rice or other cereal.

Geographical distribution.—The area of the endemic distribution of beriberi is coextensive, probably, with the tropical and subtropical belts ; doubtless it exists in many places where its presence is not generally suspected. It is the scourge of many of the mines and plantations of the Malay and Eastern Archipelago. It is apt to break out among the coolie gangs engaged on extensive engineering works in the tropics, such as the Panama Canal or the Congo Railway. It haunts the Dutch army in Sumatra, and used

Digitized by Google

to be common enough in the British armies in India. It is at home in many parts of Japan, particularly in her large, low-lying, damp, overcrowded cities. It occurs in China, the Philippines, the Eastern Peninsula, India, and Africa. It is prone to break out in jails, in schools, in ships. Sometimes, as an epidemic wave, it passes over a tropical country, as was the case in the early 'sixties in Brazil, where it still lingers. Sometimes sporadic cases crop up here and there. Generally, when it appears in a community it attacks large numbers, picking out particular houses and districts. We have had accounts of a small epidemic among a group of Western Australian natives, and also among Chinese on the eastern seaboard of Australia, a continent where beriberi was formerly supposed not to exist. Similarly it appears, apparently for the first time, in Japanese immigrants in Fiji. Some time ago, Manson saw a case having the history and clinical features of beriberi from Lake Nyasa, another from the Upper Congo, another from Hayti. We hear of it also from Havana, from New Caledonia, from the Sandwich Islands, from Uganda—all of them places not before known to be liable to this disease—so that the area of distribution is an extensive one. Indeed, within the last few years it would seem that it includes the temperate as well as the tropical zones. Not long ago beriberi showed itself in a lunatic asylum in Ireland—Richmond Asylum, Dublin; and apparently the same disease has been seen lately in lunatic asylums in the United States and in France, and also among the fishermen on the North American coast. It occurred amongst the besieged garrison in Kut during the Mesopotamian campaign, and also to a limited degree in Gallipoli.

Symptoms.—Medical visitors to the native hospitals in many parts of the tropical world are likely to have their attention arrested by the large proportion of cases of partial paraplegia, of cases of œdema of the legs, and of cases of general dropsy. These, for the most part, are cases of beriberi.

Paraplegic cases.—On examining one of the paraplegic cases referred to (Fig. 83), it will be found that, besides paraplegia of greater or lesser degree, there is a certain amount of anæsthesia or of numbness of the skin; particularly of the skin over the front of the tibiæ, the dorsa of the feet, the sides of the thighs, perhaps also of the finger-tips, and of one or two areas on the arms and the trunk. The visitor may be struck with the thinness of the patient's calves and the flabby state of the gastrocnemii; and by the fact that if, whilst making the examination, he should handle these and the neighbouring muscles somewhat roughly, particularly if he should squeeze them against the underlying

Digitized by Google

bones, the patient will call out in pain and try to drag the limb away. The thigh muscles may be found to be similarly affected, and so may the thenar, the hypothenar, and the arm muscles; like the calf muscles, these too may be wasted and flabby. Very probably there is a loss of fat as well, the panniculus adiposus being everywhere meagre. If tested electrically, the muscles exhibit to perfection the reaction of degeneration. If the knee reflex be tested in the usual way, after the first week of the disease there will be no response whatever; nor can any clonus be elicited. As a rule, all the deep reflexes are lost; but the superficial reflexes, unless in extreme conditions of paresis and muscular atrophy, are usually present and more or less active. If, in severe cases, the patient is set to button his jacket or to pick up a pin, possibly he has a difficulty about it, or perhaps he cannot; he may bungle and fumble like an advanced ataxic.

Fig. 83.—Paraplegic beriberi. (*Bentley.*)

There is more than ataxia, however, for the hand-grasp is so enfeebled that the patient may have a difficulty in holding his rice-bowl as well as in feeding himself. There is no tremor of the hands; and never or very rarely is there any paresis of the ocular muscles, or of the muscles of the face, of mastication, of the tongue, or of the pharynx. The sphincters and bladder operate satisfactorily, and the functions of the alimentary canal are carried on fairly well, although there is often some dyspeptic distension and oppression after food. On the patient being got out of bed and started to walk, if he is able to progress at all, his gait will be markedly ataxic; but he is not ataxic merely, for, just as with the hands, it will be seen that, in addition to want of co-ordinating power, there is great muscular weakness. If he is laid on the bed and asked to raise his legs, he is perhaps hardly able to get them off the mat, to cross them, or to place them one foot on top of the other. Very probably

Digitized by Google

he is the subject of marked ankle-drop, so that he drags his toes when he attempts in walking to advance the foot; he has therefore to raise the foot very high, letting it fall on the ground with a flop when he brings it down again. His ataxia and his muscular weakness, as well as the partial anæsthesia from which he suffers, force him to adopt a variety of devices to assist him in progression

Fig. 84. - Paraplegic beriberi. (*Bentley.*)

(Fig. 84). Manifestly these patients are suffering from some form of peripheral neuritis.

The general health is good for the most part; the tongue is clean, the bowels are fairly regular, there is no fever, and there is nothing amiss with the urine. Digestion, assimilation, and excretion go on satisfactorily.

The heart and circulation.—When the heart is examined, if the case be at all recent or moderately severe, attention is at once

Digitized by Google

arrested. On inspection it may be remarked that the impulse is diffuse, that there is epigastric pulsation; that the carotids throb too violently; that there is that peculiar wobbling, pulsating movement in the jugulars that denotes tricuspid insufficiency. On percussion the præcordial area is frequently found to be enlarged, perhaps very greatly enlarged, especially to the right; and on auscultation loud bruits, usually systolic in rhythm, may be heard. Marked reduplication of the sounds, particularly of the second sound, is to be noted. The auscultator may be struck, in a large proportion of cases, by the peculiar spacing of the intervals between the sounds. It may be hardly possible to tell by the ear alone which is the first pause and which is the second. They seem alike in point of duration; so that the sounds of the heart are, like the beats of a well-hung pendulum clock, evenly spaced, and not, as they are in health.

Fig. 85.—Dropsical beriberi. (*Bentley.*)

separated by a long and a short interval like the beats of a badly hung clock. It will also be observed that the heart is very irritable, becoming easily quickened by exertion. It will be judged, therefore, that, in addition to peripheral neuritis, there is serious disease in the circulatory system, particularly in its innervation; that there is dilatation of the right side of the heart; and that there is a state of relaxed arterial tension.

All these signs and symptoms vary in degree from time to time in the same case, and differ in degree in different cases.

Dropsical cases.—In the next bed, perhaps, to the patient whose picture has been drawn may be seen another man suffering from apparently quite a different affection (Fig. 85). He is propped up in bed. Instead of being thin and wasted, as the last patient, his face is puffy and heavy; his lips possibly are slightly cyanosed; and his arms, hands, trunk, legs, and feet are distended with œdema. It may be thought from the œdema that it is a case of acute nephritis, but an examination of the scanty, dark-coloured urine shows that

Digitized by Google

it is of high specific gravity and contains no albumen or only a mere trace; so that the case cannot be one of acute Bright's disease. Careful observation will discover that the œdema is somewhat firmer than that of nephritis, and, in not a few instances, that it does not involve the scrotum. Occasionally cases are met with in which the œdema is peculiarly localized and fugitive. If attention be directed to the heart, a bruit and other evidences of dilatation of the organ and of arterial relaxation, just as in the first case, are discovered. If the lungs be examined, one may (or may not) discover signs of single or double hydrothorax, although, probably, not to a very great extent. The lungs themselves are healthy. On getting him out of bed it is found that the patient can hardly walk—partly from breathlessness, partly on account of mechanical interference by the dropsy with the movements of the legs, partly, perhaps, from some degree of paresis. He has ankle-drop, possibly; and, if firm pressure be brought to bear on the calf muscles through the œdema, signs of hyperæsthesia of the muscles may or may not be elicited. Knee-jerk is probably absent, and there is numbness of the shins and finger-tips. The tongue is clean, the appetite fair, and there is no fever. But there may be complaint of præcordial distress and even pain, and, as this is aggravated by a full meal, the patient eats sparingly. The amount of urine is generally very much reduced—to a few ounces, even.

In this patient, therefore, there are the same signs of peripheral neuritis and of dilatation of the heart as in the other case. In addition, there is a somewhat firm œdema, which is not altogether cardiac, but, as its character and the circumstances in which it is found suggest, is probably connected partly with lesion of the nerves regulating urinary excretion, and partly with the play of transudation and absorption in the connective tissues.

Mixed paraplegic and dropsical cases.—In the next bed to this patient there lies, perhaps, another case which looks like a mixture of the two preceding. There is œdema—generally somewhat firm—particularly of the shins and feet, about the flanks, sacral region, and, very generally, over the sternum and root of the neck. There is numbness of the shins, there is some ataxia, there is muscular weakness and hyperæsthesia—particularly of leg and thigh muscles; there is absence of knee-jerks, there are probably a cardiac bruit and reduplication of sounds, and there are signs of dilatation of the heart and relaxed arterial tension. Just as in the other cases, the general health of the patient is unaffected, the tongue is clean, the urine though scanty is otherwise normal, and there is no fever.

Great variety in degree and combination of symptoms.—All

Digitized by Google

through the wards of the hospital similar cases may be encountered. Some are so trifling that they are up and moving about with more or less freedom; and others are so severely smitten that they lie like logs in their beds, unable to move a limb or perhaps even a finger. Some are atrophied to skeletons; others are swollen out with dropsy; and some show just sufficient dropsy to conceal the atrophy that the muscles have undergone. Though the cranial nerves above the seventh are very rarely involved, in some it will be noticed that the laryngeal muscles are paralysed, the patient being unable to speak above a whisper or to produce an explosive cough. In one or two cases the abdominal and the perineal muscles may be so profoundly paralysed that, when cough is attempted, at most a husky expiration is produced, whilst the belly is bulged forwards and the perineum shot downwards by the sudden contraction of the muscles of expiration. In practically all cases of over a fortnight's standing the knee-jerk and tendo-Achillis reflex are absent, though the latter often persists after the former has disappeared; at the very commencement of the disease these deep reflexes are exaggerated, gradually disappearing as symptoms develop, not to reappear for months, perhaps, after the patient is well in all other respects. In some epidemic outbreaks, as, for instance, in Mesopotamia in 1916, an irregular *pyrexia*, seldom exceeding 100° F., has been noted.

Erroneous diagnoses.—The novice in tropical medicine will be greatly puzzled for a time over these cases. They have been diagnosed as cardiac disease, tabes dorsalis, muscular rheumatism, progressive muscular atrophy, ascending spinal paralysis, and have over and over again been relegated to that refuge for ignorance, malaria, and called "malarial rheumatism," or "malarial paralysis," or, more pedantically, "malarial paraplegia" or "malarial neuritis," though cases of subtertian malaria rarely simulate the clinical appearance of beriberi.

If the visitor has the curiosity to examine the blood of these patients, possibly in a proportion of them he will find microfilariæ; very likely he will then think that the cases are forms of filariasis, and he may construct theories to explain how the filaria produces the symptoms. Or, if he examine the fæces, very probably in over 50 per cent. of the cases, or, in some countries, in nearly all the cases, he will find the ova of *Ankylostoma duodenale*, and probably those of *Trichuris trichiura* also. On this evidence he may conclude that these are cases of ankylostomiasis. He had better, however, not commit himself to such a diagnosis until he has ascertained how it fares with the rest of the population as regards these parasites; for he will find that the filaria, the ankylostoma, the trichuris,

Digitized by Google

and the ascaris are quite as prevalent outside as inside the hospital, and in the healthy as in the sick.

History of patients.—On inquiry the visitor will learn that most of the cases come from two or three centres where similar disease is endemic—from some particular institution, plantation, mine, or village. He will remark that the same places supply both atrophic-paralytic cases and dropsical-paralytic cases; and he will learn, besides, that many of the atrophic cases commenced with dropsical symptoms. From this he will make the important deduction that he is dealing, not with two diseases, but with two phases or clinical forms of the same disease—a disease which sometimes assumes atrophic features, sometimes dropsical features, and sometimes is of a mixed character. Some of the patients will give a history of fever at the outset of their troubles; in some there is a history of indigestion or diarrhœa; in some the paralytic or dropsical symptoms developed very slowly; in others, again, they came on rapidly. In some there is a history of a similar attack the previous year, or a yearly attack for three or four years in succession. Some will tell that they have been ill for several months; others that they have been ill for a week or two only.

Uncertain course.—The visitor will learn that this disease, which is beriberi, slowly or rapidly declares itself after an incubation period as yet undetermined but variously stated as of weeks or months; that it may be preceded by a period of intermitting languor, aching legs, palpitations, breathlessness, slowly advancing œdema of legs or face; or that the patient may wake up some morning and find that during the night he has become dropsical or paretic. Thus the disease may develop slowly or rapidly. Equally uncertain are its progress and danger; within a day or a week, or at any time during its course, it may assume fulminating malignant characters. It may completely subside in a few days, or it may drag on for months. It may get well apparently and then relapse. It may, and generally does, clear up completely; or it may leave a dilated heart, or atrophied limb muscles with corresponding deformity. The variety in the severity, progress, and duration of beriberi is infinite; but in all cases the essential symptoms are the same—greater or less œdema, especially over the shins; muscular feebleness and hyperæsthesia, especially of the legs; numbness, especially of the front of the shins, of the finger-tips, occasionally of the lips; liability to palpitation from cardiac dilatation, and to sudden death from the same cause.

Progress of the cases.—As the visitor watches the progress of the cases he will be astonished that those which he thought examples

Digitized by Google

of locomotor ataxia, or of progressive muscular atrophy, or of ascending spinal paralysis, gradually improve, begin to walk about, and finally quit the hospital quite well. He will be astonished to see, after perhaps a profuse diuresis, the bloated carcass, that could hardly turn itself in bed, rapidly shrivel to little more than skin and bone, and assume all the appearances of the atrophic cases; and later, perhaps after many months, to find the patient become rehabilitated and, in due course, walk out of the hospital quite well. He will notice that the cardiac bruits come and go; that the degree of dilatation of the heart is subject to fluctuations; that what seemed confirmed organic disease completely disappears.

Cardiac attacks.—But he will also be astonished, as he goes his rounds, to see so often empty beds where the day before lay men whom he considered by no means seriously ill—certainly not dying. Some day he will come on a patient, whom the previous day he thought to be not dangerously ill, actually *in extremis*. The poor fellow is propped up in bed, he is struggling for breath, his face is purple, his eyes are starting out of his head, his whole attitude is expressive of the utmost distress; he has a horrible tearing, boring, crushing pain under his sternum and in the epigastrium; the vessels of his neck are throbbing violently, but his pulse is quick, small, intermittent, and his extremities are cold. In a short time the patient is dead. Some of the fatal cases, he will note, die quite suddenly as if from syncope; but most die in the distressing way described, evidently from paresis and over-distension of the right heart, complicated and aggravated by œdema of the lungs, or by diaphragmatic paralysis, by hydrothorax, or by hydropericardium.

Nomenclature and classification of beriberi.—For purposes of description, the paralytic-atrophic cases are designated "dry beriberi" or beriberia atrophica; the dropsical cases, "wet beriberi" or beriberia hydrops; and those in which there is a combination of both conditions, "mixed beriberi." Sometimes the cases are classified, according to the rapidity of development and gravity of symptoms, into acute or pernicious, subacute, and chronic. None of these classifications is good, seeing that they all refer to what is clinically the same disease, and that one form may suddenly or more slowly merge into the other.

Etiology. *Sex, age, occupation, etc.*—Beriberi attacks both sexes. It is not uncommon in the breast-fed infants of beriberic mothers. This form, called infantile beriberi, may declare itself in varying ways: the child may become aphonic, or extremely restless with incessant crying, or may exhibit signs of subacute

Digitized by Google

meningitis, drowsiness, head retraction, and rotation of the eyes. It is rare in childhood and extreme old age, its favourite age being from about 15 to 30. It affects rich as well as poor. It is confined to no particular trade or occupation. If anything, it has a predilection for those who lead a sedentary life and are much indoors, as students, prisoners, and the inmates of hospitals and asylums. It is apt to attack pregnant or parturient females. It is quite as common in the strong and full-blooded as in the weak and anæmic.

Climatic conditions.—In countries in which there are a hot and a cold season the epidemic outbreaks occur during the former, old cases improving and new cases ceasing to crop up during the winter. In countries which are hot all the year round, beriberi may appear at any time; most frequently, however, in such climates it appears during the rains. Thus it resembles malaria in being fostered by damp and by high temperature, and, it has been said, in its most often attacking those who sleep on or near the ground. As with malaria, though its explosion in any given individual residing in the endemic area may be elicited by fatigue, chill, privation, and other causes of physiological depression, it is not actually caused by such circumstances. Unlike malaria, it is common enough in the midst of large cities, as well as in villages and jungle lands.

Influence of overcrowding.—Overcrowding and unhygienic conditions generally seem to favour the outbreak, or possibly the spread, of beriberi. This has, perhaps, a good deal to do with its frequency and virulence in oriental jails, schools, mining camps, plantation lines, armies, ships.

Ship beriberi.—Unlike malaria, beriberi is common in the native crews, more rarely, though occasionally, among the European officers and sailors, of ships on the high seas and far away from any recent telluric influence. The crowding in the damp forecastle and the exposure incident to a sailor's life seem to be among the reasons, though not the only ones, for ship beriberi. The fact is that some of these epidemics of ship beriberi occurring in cold climates are fostered, though they may not be caused, by the artificial conditions which the ignorant lascars are allowed to bring about. They feel the cold of the English climate so much that, on entering British seas, they try to keep their quarters warm by lighting fires and stopping up ventilators. By these means they create a hot, steamy atmosphere and a sodden state of the place they live and sleep in, which is a very good imitation of the tropical conditions in which beriberi is prone to develop. Although such unhygienic conditions favour the occurrence of beriberi, they do not suffice to produce it,

Digitized by Google

as is proved by the well-authenticated circumstance that since 1894 the disease has been common in the European crews of Swedish and Norwegian ships, which, as compared to British ships, are in far better sanitary condition, and yet beriberi is comparatively rare in the latter. The modern explanation of this occurrence is found in the fact that, since the promulgation of a law at the date above-mentioned, the crews of the Norwegian mercantile marine have been provided with bread baked from white flour, or a mixture of wheat and rye—in other words, a dietetic explanation.

Asylum beriberi.—Exactly similar conditions to those above described, and with similar results, were conduced to, not necessarily caused, by similar circumstances in the Dublin lunatic asylum already alluded to. This asylum, built for 1,000 inmates, had 1,500 crowded into it. Anyone who knows what the atmosphere of even a well-regulated and not overcrowded dormitory in a lunatic asylum is like can imagine what it becomes in warm weather, when three patients are lodged in a place barely sufficient for two. The heat, the breath vapour condensed and streaming down the walls, the effluvia from the patients, the closed doors, the barred windows, the want of air, and the damp conspire to reproduce the conditions found in the tropics; and it may be that when such conditions are reproduced elsewhere, even in temperate climates, the result will be just the same.

Food-deficiency theory.—Although for a long time something had been known about the conditions predisposing to beriberi, it is only lately that anything like approximately accurate knowledge as to the *causa causans* of the disease has been attained. Many hypotheses had been advanced on the subject, some plausible enough if judged of in the light of the times, others manifestly absurd. It is unnecessary to refer at length to these exploded theories. Suffice it to say that their authors appear for the most part to have been dominated by the idea that for the production of a disease something in the nature of a germ or of a poison has to be introduced into the body; they overlooked the possibility of disease being brought about, not by the introduction of something foreign or abnormal into the body, but by the deprivation of something essential for its healthy nutrition. We now know that it is to the latter circumstance we have to look for the cause, or at least a principal part of the cause, of beriberi. Beriberi is a disease of "deficiency," to use the expression of Funk.

It is desirable, in view of the possibility of further discovery, somewhat to qualify this statement. It is just possible that the condition brought about by this deficiency merely predisposes to,

Digitized by Google

or is necessary for, the operation of something else, perhaps an unknown germ which in the absence of this deficiency would remain inoperative even if introduced. Further, it may be that there are two or more diseases included under the term " beriberi," each of them acknowledging a different specific cause. Indeed there are not a few facts suggestive of such a possibility.

However this may be, thanks to the pioneer work of Eijkman, Braddon, Fraser and Stanton, we now know that the beriberi of the Eastern Peninsula, of the Eastern Archipelago, of the Philippines, of China and Japan, is a sequel of a diet into which over-milled rice enters as the principal element, that is rice from which the entire pericarp and germ have been removed; and that in this pericarp and germ there is a substance essential for the proper nutrition of the nervous system of man and of many other warm-blooded vertebrates.

If a fowl be fed on *paddi* exclusively, that is rice from which the husk has not been removed, the fowl will thrive and very likely gain weight; but if it be fed on a diet exclusively of white rice, that is rice from which the pericarp has been completely removed, it will after a short time show signs of peripheral neuritis, lose weight, and, if the exclusive diet be persisted in, die with all the signs of a multiple peripheral neuritis. If a fowl which, in consequence of such a diet, has begun to show signs of peripheral neuritis be given regularly some of the polishings of the rice, that is the dust or remains of the pericarp, which had been removed in the process of milling, it will gradually lose the signs of neuritis, gain in weight, and recover. The neuritis—*polyneuritis gallinarum*, as it is called —is evidently the result of the deprivation of some element of food essential for the proper nutrition of the nervous system of the bird, and this element is located in the pericarp and germ of the rice grain (Figs. 86, 87). Almost miraculous recoveries in the stricken birds take place after hypodermic injection of an extract of the germ centre of wheat or other cereal.

The polyneuritis of the fowl is identical clinically and, possibly, etiologically with the polyneuritis, called beriberi, occurring in man. For, as has been both accidentally and intentionally done, if the same experiment with rice-feeding is tried on man, the result is identical—beriberi is induced. Thus, Strong and Crowell conducted a series of experiments on twenty-four life-sentenced prisoners, and were able to prove (*a*) the non-communicability of the disease and (*b*) its production in man solely by means of diet. A similar condition has been produced in rats.

Fraser and Stanton showed—and their observations have been

Digitized by Google

abundantly confirmed—that the antineuritic element is located in the pericarp of the rice grain, in the aleurone layer and in the embryo of the grain, that it is soluble in water and alcohol, is stable in acid but unstable in alkaline solutions, is thermolabile—being destroyed by a temperature of 130° C.—and that it is dialysable; that it is not a phytin nor a fat, and that, although itself not

Fig. 86. — Showing the various stages in milling of the rice grain. (*After Chick and Hume, from "Trans. Soc. Trop. Med. and Hyg."*)

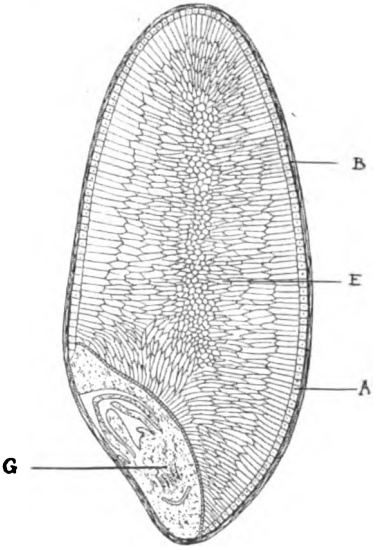


Fig. 87.—Diagram of longitudinal section through a grain of wheat, showing (A) aleurone layer of cells forming the outermost layer of the endosperm, removed with the pericarp during milling; (B) pericarp forming the branny envelope; (E) parenchymatous cells of the endosperm; (G) embryo or germ. (*By permission of H.M. Stationery Office, from Dr. J. M. Hamill's Report on the Nutritive Value of Bread made from Different Varieties of Wheat.*)

containing phosphorus, the amount of phosphorus in any given rice is a reliable indication of the safety, or otherwise, of that rice as a staple article of food. Rice containing less than 0·4 per cent. of P_2O_5 they consider unsafe, and believe that its persistent use may lead to beriberi.

Acting on these findings, the Governments of Singapore and the Federated Malay States interdicted the use of white or polished rice

Digitized by Google

in their jails, lunatic asylums, schools, and hospitals, with the result that beriberi, which until then had been the cause of an enormous mortality and morbidity, has been practically banished from these institutions. Corresponding results have accrued from the same practice in Dutch Malaya, in the Philippines, and elsewhere.

It has been proved by Funk and others that the same or a similar antineuritic body is present in other cereals and in a variety of foodstuffs. It seems probable that the destruction by heat in the process of canning, or otherwise, of this accessory factor, called by Funk " vitamine," the water-soluble B substance of McCollum and Davis—which exercises a curative as well as a protective action—may account for the prevalence of ship beriberi in Scandinavian ships, especially in long voyages during which such foods are an unavoidable necessity. In this respect there is a parallelism between beriberi and scurvy.

The period of development of beriberi in man has been determined by Fraser and Stanton as varying between eighty and ninety days.

Vitamines.—This subject is one of increasing importance and great magnitude. In a book such as this it is only possible to touch briefly upon the salient facts; for further information the reader is referred to papers by Misses Chick and Hume,* a lecture by F. G. Hopkins,† and to the exhaustive Special Report of the Medical Research Committee, No. 38, 1919. Vitamines are widely distributed amongst foodstuffs. Though small in quantity, their influence upon metabolism is great; they are regarded as not being concerned so much with the structure of tissues, but rather in the nature of stimulants or catalysts. As for their chemical nature, this cannot at the present moment be stated with certainty; originally they were regarded as being allied to allantoin. At least three of these substances are known, two of which are essential to nutrition and are called *fat-soluble A*, concerned with prevention of rickets, and *water-soluble B*, or the anti-neuritic factor, concerned with the prevention of beriberi; both are comparatively unstable, being destroyed by prolonged heating at a temperature over 100° C. The third factor, which is present in fresh vegetables and fruit, is very sensitive to desiccation, and is destroyed by a temperature of 55° C.; it is known as the *antiscorbutic factor*.

History of the discovery of anti-beriberi vitamines.—Eijkman, in 1897, in Java, was among the first to show scientifically that beriberi was connected with a rice dietary. He showed that prisoners fed on red rice escaped beriberi, and that those fed on white rice were exceedingly prone to the disease; he further found that the fowls of the establishment also developed paralytic symptoms when fed on this decorticated grain. Braddon, fixing his attention on the remarkable and admitted fact that of the various races inhabiting the Malay Peninsula the Chinese are much the most subject, the Klings (an immigrant Indian race) much the least subject to beriberi, came to the conclusion

* *Trans. Soc. Trop. Med. and Hyg.*, July, 1917; Vol. X., No. 8.

† *Brit. Med. Journ.*, April 26, 1919, pp. 508-10.

Digitized by Google

that the excessive liability of the one race and immunity of the other are attributable to the difference in the way in which their staple food—rice—is prepared for the market. The Klings live on what Braddon calls "cured rice," that is rice which when garnered, and before husking, is boiled and dried. The Chinese use "uncured rice," that is rice that is husked without preliminary boiling. That there is no racial insusceptibility in the Klings is proved by their being attacked by beriberi when they chance to get imprisoned and are placed on the same food as their Chinese fellow-prisoners. These views received support from a carefully conducted experiment by Fraser and Stanton, who fed a gang of coolies on cured rice and another gang on uncured rice, both sets of coolies being in other respects under apparently identical conditions, with the result that many of those on uncured rice sickened with beriberi, whilst those on cured rice escaped the disease.

The later researches of Schaumann, Vedder, Chamberlain and Funk, Chick and Hume, have further confirmed the views of the pioneer workers, and they have now produced beriberi in rats and other animals by depriving their food of the antineuritic vitamines. McCarrison has made out a relationship between the hypertrophy of the adrenal glands in the experimental animals and the occurrence of polyneuritis, and finds that these glands are increased to two or three times the normal weight.

Fat-soluble A is synthesized by the plant and is found in green leaves and in the embryo of many seeds, where it is present probably in loose combination with some cell constituent. Treatment of ruptured seeds with alcohol and subsequently with ether will remove the fats together with the fat-soluble accessory substance. This is present in cod-liver and various fish oils, and in beef fat and butter; on the other hand, vegetable-seed oils are deficient in the principle.

Water-soluble B.—It is now widely believed that the water-soluble B and the antineuritic factor are identical. The conclusion is drawn from the similarity and distribution of the water-soluble B factor, in experiments on rats, compared with the antineuritic factor established by experiments on pigeons. This substance is contained in the cuticle of the husked grain, in the outer or *aleurone* layer of endosperm which is removed during milling, but the richest source lies in the germ or embryo of the cereal which is removed with the bran during the process of steam milling of rice. Next to cereals the pulses, even dried peas and beans, contain the most valuable store of this substance, especially a Chinese bean, "Ratjang-idjo," *Phaseolus radiatus*. Eggs and yeast are rich in this accessory factor; the latter is especially useful, as it can be extracted in a commercial preparation known as *marmite*. Fresh meat, on the other hand, is comparatively deficient; the same may be said of butter and fat, fish, tinned meats, cheese, and vegetables. Miss Hume states that 1 grm. of *marmite* and 1·5 grm. of wheat-germ added daily to a vitamine-free diet prevent polyneuritis.

The *antiscorbutic factor* is contained mostly in fresh vegetables, cabbage leaves, juice of swedes, and the juices of citrous fruits, especially the lemon and orange; the juice of fresh limes is inferior. The essential factor is absent from both vegetables and fruit in the dried condition. Milk and meats contain very small quantities, and eggs, cereals, malt, preserved lime-juice, autolysed yeasts, pickles, little or none at all.

Food-deficiency theory not invariably a satisfactory explanation.—It is wise to sound a caution at the present moment, that the food-

Digitized by Google

deficiency theory may not satisfactorily account for every outbreak of beriberi. That overcrowding, filth, and moisture are predisposing factors in the development of beriberi is hardly open to doubt, as already stated (p. 347). Possibly infective forms of polyneuritis occur in association with the food-deficiency disease. These may account for the sporadic febrile cases already alluded to, and also for isolated outbreaks not associated with a faulty dietary. There are records from India and South America which point in this direction. One such outbreak which has been carefully investigated occurred amongst British troops at Basra in 1917. There was no evidence that it was in any way connected either with a deficient dietary or with faulty methods of cooking. The troops, in fact, were drawing the same rations as in other camps where the disease did not make its appearance.

McCarrison has noted that experimental pigeons in the pre-beriberi state—a state, that is, in which they do not exhibit any of the more alarming symptoms of beriberi—are much more susceptible to extraneous infections; for instance, an infection of *B. suipestifer* may determine the onset of the disease. It is not unreasonable to suppose that in man a microbic factor similarly plays a part in the spread of epidemics of polyneuritis which cannot otherwise be accounted for. Thus, Manson has recorded his opinion of the infectiousness of certain types of beriberi, and he quotes several instances of patients who successively occupied the same bed developing the disease.

Morbid anatomy and pathology.—There is very little to be said about the post-mortem appearances in beriberi which is not covered by the accepted descriptions of the lesions of peripheral neuritis. There is a degeneration of the peripheral nerves—more especially of their distal ends, and there is secondary atrophic degeneration of muscle, including that of the heart, which may be the subject of an acute fatty degeneration like that of diphtheria. Hamilton Wright has shown that degenerative nerve changes (formerly denied) may be detected in the nerve centres and throughout the implicated neurons, as in other forms of peripheral neuritis. There is invariably an involvement of the vagus, with degenerative changes in its root in the floor of the fourth ventricle. Microscopically the nerve trunks show changes from a slight medullary degeneration to complete destruction of the nerve (Wallerian degeneration). If there is anything peculiar about the post-mortem appearances in beriberi, it arises from the somewhat special implication of the central and peripheral organs of the circulation—namely, dilatation of the heart, especially of the right side, and great accumulation of blood in the right heart and in the veins. In addition, there is a marked liability in many cases to serous effusion into the pericardium, pleural cavities, peritoneum, and cellular tissue. This very marked liability to serous effusion and the tendency to cardiac dilatation may be said to be more or less distinctive of beriberic as compared with other forms of multiple neuritis. The type of œdema

Digitized by Google

indicates that it depends especially on vaso-motor disturbances, although cardiac weakness and partial suppression of urine may be contributory elements. Œdema of the lungs also is not uncommon, and has, probably, a pathology similar to that of the connective-tissue œdema. There is no nephritis. The only lesion that might be considered specific in beriberi is the duodenitis, which may be present in acute cases during the first three weeks of the disease, though this is not invariable.

Mode of death.—The most practically important point in the pathology of beriberi is that which relates to the modes of death. The paresis and the atrophy of the voluntary muscles, the œdema of the connective tissue, and the serous effusions are, as a rule, not very serious matters—at all events as affecting life. But it is very different when paresis and degeneration seriously implicate the heart and the muscles of respiration. In nearly all beriberics there is heart trouble, arising, doubtless, from implication of the pneumogastric nerve and the cardiac plexus. In some patients the degree of implication is slight, but in others it is sufficient so to weaken the heart that death is inevitable. We cannot be quite sure in which cases the implication of the pneumogastric nerve or cardiac plexus is likely to be serious, or in which cases it is likely to be slight. Often the mildest cases of beriberi, as judged by the degree of voluntary-muscle paresis or by the amount of œdema, are in reality the most dangerous. There appears to be an element of chance determining the nerves which the degeneration picks out. Sometimes one may see a patient who is completely paralysed so far as legs and arms are concerned, and perhaps wasted to a skeleton, and yet this same patient may never have a serious symptom referable to his heart, or in any way threatening life. On the other hand, one may see a patient with very little paresis, very little œdema, and yet in a short time the heart may become involved, and he will die in a few minutes or hours.

It is to be presumed that the dilatation of the heart, the usual cause of death, is favoured or brought about by a concatenation of several conditions: by degeneration of muscle fibre following nerve destruction, by imperfect systole in consequence of an interrupted nerve supply, by obstruction to capillary circulation in consequence of vaso-motor paresis in the pulmonary and general circulation. Once commenced, the cardiac dilatation tends to increase automatically; for the more the organ dilates the more difficult does it become for it to contract, the greater is the incompetency of the valves, and the more the blood stagnates in and over-distends it. The organ enters on a vicious pathological circle. Finally it becomes so distended that, like an overstretched bladder, it loses the power to contract altogether. The blood

Digitized by Google

then rapidly accumulates in the great veins, the right auricle and ventricle are distended almost to bursting, and death is inevitable. The result is often contributed to by the coexistence of pleural effusion, hydropericardium, paresis of the diaphragm, over-distension of the stomach by food or gas, and, above all, by œdema of the lungs. It can readily be understood how the establishment of any additional obstruction of this description would still further tax the dilated, enfeebled heart and determine the fatal issue.

When we come to make a post-mortem in these cases we may find a heart slightly hypertrophied and enormously dilated, the right cavities distended with blood, the lungs and liver full of dark blood, and all the great veins engorged.

Prognosis.—This tendency to dilatation of the heart is the dangerous element of beriberi; it should always be before our eyes and dominate our plans of treatment. It is wonderful how rapidly it may come on, and how rapidly it may prove fatal. These sudden deaths, occurring sometimes from syncope—from instantaneous failure, as well as from the somewhat slower process of increasing over-distension—are constantly sprung on one in this disease. An absolutely favourable prognosis, therefore, ought never to be ventured on in even the mildest-looking case of beriberi, or so long as the patient is exposed to the conditions causing the disease, or so long as the neuritis appears to be active. That is a lesson which is often, and sometimes painfully, borne in on the practitioner in beriberi districts.

Evidences of grave heart-implication, such as pulsating cervical vessels, equal spacing of the intervals between the sounds audible on auscultation, enlargement of cardiac dullness, especially to the right, epigastric pulsation, a rapid feeble pulse, a distended stomach, cold extremities, cyanosis, dyspnœa, and a disproportion in the strength of the heart- and wrist-beats, are significant of danger. *Paralysis of the diaphragm, of the intercostal muscles, extensive serous effusions, very scanty urine* are also unfavourable signs.

Vomiting.—No one can say when or how soon fatal implication of the pneumogastric and other cardiac nerves may take place, but vomiting is always an ugly and threatening symptom in beriberi; it probably indicates that the former important nerve is being attacked. The Japanese regard the occurrence of vomiting as of fatal import. Marked dilatation of the stomach has a similar significance.

Prognosis is improved if the patient is placed on a non-beriberic diet and is removed (that is before the heart-muscle, or the cardiac

Digitized by Google

or respiratory nerves, are gravely degenerated) from the place in which the disease was contracted to a healthy, non-beriberic, high-lying locality.

Mortality.—The mortality in beriberi varies in different epidemics and in different localities. On the whole, it is greater in low than in high latitudes, in the dropsical than in the atrophic forms, in the acute than in the chronic. In some epidemics it is as high as 30 per cent. of those attacked; in others as low as 6 per cent., or even lower.

Diagnosis.—Usually the diagnosis of beriberi is not difficult. Multiple peripheral neuritis occurring as an epidemic, or in a place or ship in which the disease has occurred on some previous occasion, may as a rule be set down as beriberi. Sporadic cases may be difficult to diagnose, especially if there is a history of alcoholism, of malaria, or of drugging with arsenic. The presence, actual or past, of œdema—especially of œdema over the shins—and palpitations and other evidences of cardiac implication, are significant of beriberi. In the atrophic or paralytic type the *jongck* or "*squatting test*" is very useful. The patient with his hands on top of his head is unable to assume or arise from a squatting position. It must be borne in mind that slighter degrees of beriberic poisoning, evidenced only by slight anæsthesia of the prætibial skin area, by slight œdema of the same region, by slight hyperæsthesia of the calf muscles, and, perhaps, by impairment or absence of knee-jerk, may be the only symptoms present. True rheumatism is rare in the tropics. Among natives, especially if their language is not understood, complaints of what may seem to be rheumatic pains in the legs should always be carefully investigated, the knee-jerks tested, and signs of hyperæsthesia of the calf muscles sought for. The significance of these signs of what may be described as larval beriberi is too frequently overlooked until some sudden death, which, with earlier recognition of the disease, might have been avoided, puts the practitioner on his guard. All paretic affections, all cases of œdema, all cases of palpitation, and all cases of rheumatic-like pains occurring among the natives of warm climates, therefore, should suggest the possibility of their being beriberic, and also the necessity for a detailed examination with this in view. Arsenical neuritis, arising from the presence of this poison in beer or in food, may simulate beriberi very closely. There are several instances on record of epidemics of beriberi, erroneously diagnosed as such by experienced observers, which have been proved to be arsenical by the discovery of this metal in the hair. Beriberi must be distinguished from ankylostomiasis and nephritis. Its

Digitized by Google

differentiation from tabes and from œdematous scurvy should present no difficulty. The significance of a polyneuritis due to absorption of diphtheritic toxins, or of toxins from desert or veld sores, must not be lost sight of (p. 699); these cases may simulate beriberi very closely.

Treatment.—The first and most important thing to be attended to in the treatment of a case of beriberi is the diet. From this, rice, especially white rice, should be eliminated, and some article rich in vitamine—such as beans, peas, peanuts, barley, wheaten flour (not over-milled), or oatmeal—substituted, and, in view of the fact that as yet we cannot be certain that beriberi is not in some way dependent on an unknown germ, the patient should be removed, if practicable, to some place away from the endemic spot, to some dry locality, if such is available. He should sleep well off the ground in a thoroughly ventilated, sunny room situated in an upper storey. He ought to clothe sufficiently and feed well, taking care that the food is of a varied and not of a bulky character, and that it contains a sufficiency of nitrogenous and fatty elements. Apart from other considerations, rice is a bad food for beriberics; it is too bulky. Eggs are valuable sources of the anti-beriberi factor, which is not destroyed even when they are dried; they are therefore indicated. Yeast has curative properties; the extract known as *marmite* may be given in doses of 1·5 grm. daily. Animal food, including fat and milk, must enter into the dietary for general nutritional purposes. The worst cases, particularly if there is any sign of serious cardiac implication, should remain in bed; but the mild cases had better spend the greater part of the day in the open air. If the disease break out on shipboard the dietary should be changed and the crew should be kept out of the forecastle and, so far as possible, made to sleep on deck, properly protected from the weather by an awning.

With a view to diminishing to some extent the bulk of blood in the vessels and heart, the seriously affected patients should take little fluid, and keep the bowels free by means of full and repeated doses of some saline aperient. In cardiac cases small doses of digitalis or of strophanthus seem to do good. Should signs of acute cardiac distress appear, full doses—three, four, or five drops of the 1-per-cent. solution—of nitro-glycerine are indicated. The dose must be repeated every quarter- or half-hour, and kept up until the threatening symptoms pass away. In suddenly developed cardiac attacks inhalations of nitrite of amyl, pending the operation of the nitro-glycerine, may be given. It is well for these two drugs to be in the hands of properly instructed ward attendants, so as to

Digitized by Google

meet cardiac complication on its earliest appearance. There is often no time to send for the doctor. Should signs of cardiac distension and failure persist and increase in spite of these means, there must be no hesitation in bleeding the patient, taking, if it will flow, eight or ten ounces from the arm, or, this failing for any reason, from the external jugular. Often, as the blood flows, rapid amelioration of the alarming condition sets in, and the patient is, for the time being, tided over an acute danger and given another chance. The bleeding should be repeated if the alarming symptoms recur, as they are almost sure to do. Oxygen inhalations, if available, are worth trying in cardiac attacks. Pleural and pericardial effusions should be sought for, and, if deemed to be interfering in the slightest degree with the circulation or respiration, drawn off with the aspirator.

Provided the patient is placed on a suitable diet and has been removed from the spot where he fell ill, and provided he can be tided over the first fortnight, he will probably recover; but, on the other hand, should he persist in a diet of white rice and remain in the place where his disease was acquired, though he may get over one or two cardiac attacks, he will almost surely die.

In the case of breast-fed beriberic infants, they should be removed from the mother and handed over to a healthy wet-nurse, or placed on the bottle. Sometimes this is impracticable; in such cases in the Philippines a preparation of extract of rice-polishings, called "tiqui-tiqui," has the reputation of being wonderfully efficacious. It is given to the extent of 5 c.c. a day in 20-drop doses every two hours. At the end of twenty-four hours the most alarming symptoms disappear, and the child is well in three days. If the case is a very severe one double doses should be given, and the tiqui-tiqui continued so long as there is any aphonia.

For the atrophy of the muscles and anæsthesia of the skin, faradization and massage are of service, and should be employed as soon as the muscular hyperæsthesia has begun to subside. Strychnine, arsenic, and nitrate of silver are in repute as tonics in these circumstances. Care should be taken that permanent deformity does not occur from contraction of muscles. Foot-drop should be counteracted by Phelps's talipes splint with an elastic accumulator, and any other threatened deformity appropriately met. Relapses must not be risked by a return to the original diet or source of infection. The seaside or a sea-voyage has often a marvellously restorative effect.

Prophylaxis.—When beriberi breaks out in a school, jail, or similar institution the place should be emptied of its inmates as soon

Digitized by Google

as possible ; at all events, those parts of the building in which the disease has appeared ought to be cleared out, and not re-occupied until they have been thoroughly cleansed, disinfected, ventilated, and dried. Overcrowding must be strictly avoided. Ventilation must be effective. The dietary should be revised, and, if necessary, rice should be eliminated ; it may be replaced by meat, flour, or beans. All the inmates should be obliged to pass the larger part of every day in the open air ; their knee-jerks should be tested, and their legs examined for numbness, œdema, and muscular hyperæsthesia from time to time. Any suspicious case should be removed at once.

Should beriberi appear on board ship, besides the precautions already indicated, on the assumption that there may be an infective as well as a dietetic element at the bottom of the disease special means of disinfection must be employed. Rotten planking and bilge-water must be removed from the neighbourhood of the quarters of the crew ; the sound woodwork should be scraped and painted ; disinfectants should be freely and frequently employed ; clothes and sea-chests washed and disinfected.

In beriberi countries, low-lying, damp situations should be avoided as building sites. The sleeping quarters, especially, should be raised well off the ground and located, if possible, in an upper storey ; all rooms should be so arranged as to be easily flushed with fresh air and flooded with sunlight.

As yet we know little of the virus of beriberi, if such there be, nor is our knowledge of the way in which it is acquired by any means complete. It may be communicable, and until we have more precise knowledge it is unjustifiable not to recognize the subjects of the disease as being possible sources of danger to others. Therefore, in the endemic zone, beriberics should be treated as infective and isolated. In jails and similar institutions new-comers, whether manifestly suffering from beriberi or not, should be isolated and kept under special observation for a time, their clothes disinfected and body vermin scrupulously destroyed. Prison clothes and prison blankets especially should always be disinfected before being passed into store and before being served out. The utmost care should be exercised to keep prisoners free from vermin, and the premises from flies, cockroaches, fleas, bugs, and all insects that might possibly serve as transmitters of the hypothetical virus.

In institutions under Government control, or in conditions in which it can be successfully enforced, there should be a stringent rule against the use of over-milled rice. To legislate against the use of white rice in countries in which rice is the staple food would

Digitized by Google

not be politic, and could only lead to opposition and defeat the object in view; but the authorities, by educative methods and in other ways, can do much gradually to eradicate any prejudice there may be amongst the natives against under-milled rice.

As a prophylactic, *marmite*, in small ¼-oz. cubes, may be taken twice a week. Military and other expeditions should be warned that tinned meats are notably deficient in antineuritic vitamines and require the addition of other foodstuffs to protect against beriberi.

Vedder is of the opinion that in arranging a diet to prevent the onset of beriberi it is sufficient to ensure the consumption of the amount of antineuritic foodstuffs (beans, rice-polishings, etc.) without reference to the amount of carbohydrate consumed.

Contrary to what happens in scurvy, the human body does not appear to possess any appreciable reserve store of the antineuritic vitamine upon which to draw in an emergency. A constant supply, therefore, of the substance must always be maintained. The moral of this is, that for the prevention of beriberi for any population living on a restricted diet, such as soldiers on active service, the germ and bran of wheat should be included in the manufacture of bread or biscuit where the rest of the ration consists of tinned foods.

Digitized by Google

CHAPTER XXV

EPIDEMIC DROPSY (WAR ŒDEMA)

Definition and description.—An epidemic disease, running its course in from three to six weeks, and characterized by the sudden appearance of anasarca, preceded in most instances by fever, vomiting, diarrhœa, or by irritation of the skin, and often accompanied by a rash, by fever of a mild, remitting type, by disorder of the bowels, and by pronounced anæmia. The case-mortality varies from 2 to 40 per cent., death being sudden and depending upon œdema of the lungs, hydrothorax, hydropericardium, or other pulmonary and cardiac complications.

History and geographical distribution.—The disease first attracted notice in Calcutta in the winter of 1877–8. Since then it has made sporadic appearances, always vanishing with the advent of the hot season. In Mauritius it prevailed in 1879 and attacked about one-tenth of the coolies, of whom 729 died. A limited epidemic appeared in Calcutta in 1901, and again in 1908–9. This is probably the same disease as *war œdema*, which was noted in Central Europe (especially in Vienna), Palestine, and East Africa during the recent war.

Etiology.—Both sexes are attacked; children under puberty are less liable than adults; sucklings are seldom affected. The weak and the robust are equally susceptible. There are no direct observations on the germ of the disease, but there is indirect evidence of its portability and communicability.

Greig, who made a special study of the disease during the epidemics in Calcutta, concludes that in many ways epidemic dropsy resembles ship beriberi. Observations on war œdema seem to indicate that deficiency of fats in the dietary plays a part in its causation; others regard it as due to a deficiency of calcium salts. Bigland, Enright, and the Editor, from observations upon œdema in Turkish prisoners of war, have been unable to trace any connection between the œdema and any antecedent disease such as dysentery, malaria, or pellagra. It must be remembered, however, that diminution in the circulating protein, by decreasing the osmotic pressure, may lead to œdema of the tissues; for instance, Eckstein has demonstrated the importance of this

Digitized by Google

factor in the œdema so characteristic of chronic parenchymatous nephritis.

Identification.—McLeod, after a careful analysis of all the available evidence, concluded that epidemic dropsy was a disease *sui generis*. At the time of its occurrence in Calcutta many of the physicians there looked upon it as a form of beriberi; and, indeed, in many respects it resembles very closely those cases of beriberi in which dropsy is a prominent symptom, and in which the nervous phenomena are slight or altogether absent. But in epidemics of beriberi such cases are the exception—in fact, are very rare, and always are concurrent with others in which nerve symptoms are pronounced, and with purely atrophic cases; such were not seen in either the Calcutta or the Mauritius or the Turkish epidemics.

Special symptoms.—Dropsy is almost invariably present. It usually appears first in the legs, and in some instances is confined to the lower extremities; in others it spreads and involves the entire body. Occasionally it is very persistent, lasting and recurring during convalescence. Fever also is a very constant symptom; sometimes it precedes, sometimes it accompanies, sometimes it succeeds the dropsy. It is rarely high, ranging usually from 99° to 102° F.; in a few cases—possibly from malarial complications—it reaches 104°. Rigors are rare. Diarrhœa and vomiting generally ushered in the disease in the Mauritius epidemic. In Calcutta these symptoms were not so frequent, although they were by no means rare there, occurring at both the earlier and later stages. Dysentery was common in the Calcutta epidemic.

Nervous symptoms—such as burning, pricking, itching, and feelings of distension of the skin, sometimes limited to the soles and feet—often preceded the dropsy; and distressing aching of muscles, bones, and joints, worst at night, was usual. Anæsthesia of skin areas and paresis of muscles were never observed in Mauritius. The knee-jerk is not abolished. An exanthem, erythematous on the face, rubeolar on the trunk and limbs, was frequently seen in Mauritius, less frequently in Calcutta. It appeared about a week after the œdema, and lasted from ten to twelve days. Disturbances of the heart and circulation were prominent features in nearly all the cases. The pulse was weak, often rapid and irregular, blood-pressure low; cardiac bruits were also noted. Breathlessness on exertion occurred in all cases, severe orthopnœa in many. Signs of pleural and pericardial effusion, of œdema of the lungs, of pneumonia, and of cardiac dilatation were common in Calcutta. Anæmia was usually present and marked; so were wasting and

Digitized by Google

prostration. Scorbutic symptoms occasionally showed themselves. The liver, spleen, and kidneys were not specially affected. The urine was not albuminous.

Morbid anatomy.—Beyond general œdema and occasional pleural and pericardial effusion, nothing special was remarked post mortem. There is said to be a diminution in the amount of albumen in the body, and a general wastage of all organs, including the endocrine glands.

Treatment.—An analysis of the albumen-content of the blood will serve as an indication for the administration of albumen per os. Egg and milk albumen are indicated in large quantities if such a deficiency is demonstrated.

Digitized by Google

CHAPTER XXVI

PELLAGRA

Synonyms.—Pellarina; Mal de la Rosa; Mal Rosso; Flema Salada; Alpine Scurvy; Asturian Leprosy; Asturian Rose; Disease of the Landes; Dermotagra; Psilosis Pigmentosa.

Definition.—An endemic disease of slow evolution, characterized by a complexity of nervous, alimentary, and cutaneous symptoms, which make their first appearance during the spring months (sometimes the autumn months), and recur year after year at the same season, remitting more or less during the winter months. It is for the most part confined to the poorer classes, especially agricultural labourers. The more distinctive features are—(*a*) a remitting dermatitis of the exposed parts of the body; (*b*) marked emaciation; (*c*) profound depression alternating with mania.

Geographical distribution.—*Europe:* Pellagra has a wide distribution in Southern Europe. It is found in northern Portugal, in Spain, in Italy, in the south-west of France, in the Austrian Tyrol, in Hungary, Croatia, Dalmatia, Bosnia, Servia, Bulgaria, Turkey, Greece, Corfu, Rumania, Bessarabia, Kherson, Poland. Sambon has shown that, though hitherto practically unrecognized, it prevails endemically throughout the British Isles.* *Africa:* Algeria, Tunis, Egypt, the Red Sea coast, Rhodesia, Nyasaland, and among the Kaffirs and Zulus. Sandwith found it in 1900 among the coloured lunatics on Robben Island. *Asia:* It has been reported from Asia Minor and North Behar in India (Ray, 1902), Singapore, Philippine Islands. Pellagra was especially prevalent in Turkish troops and Armenian refugees during the recent war, in Palestine and Syria. *America:* The United States, Mexico, Central America, Brazil, the Argentine, Barbadoes, and

* Until 1912 pellagra was not known to be endemic in the British Islands. It is true that three or four cases had been described and correctly diagnosed between 1863 and 1909, but they had not attracted any attention. Indeed, Sandwith, who had had the opportunity of studying pellagra in Egypt, stated that the published accounts did not tally with the disease as he knew it, though the symptoms were somewhat similar to those of pellagra. Since 1912 Sambon has had the opportunity of examining over a hundred cases of indigenous pellagra in England, Scotland, and Wales, and he has established that pellagra is widely distributed throughout the British Isles, having endemic stations as far north as the Shetlands. He also believes that the disease is of long standing in these isles, as evidenced by the Spanish-derived name of "the rose," still used in Scotland to indicate pellagra and other easily confounded erythematous conditions of the exposed parts.

Digitized by Google

probably in other West India Islands. *Australasia :* Neirte has reported it in New Caledonia.

History.—The history of pellagra is comparatively recent. The disease was recognized and described almost simultaneously in Italy and Spain. In Spain it was first described by Casal in 1762 under the name of *mal de la rosa.* In Italy the disease, under the name of Alpine scurvy, was described by Odoardi in 1776. Frapolli, who described the disease in 1771 under the name of pelagra (*sic*), says that probably it is the same as pellarella, a disorder mentioned as early as 1578 in the rules of admission to the Ospedale Maggiore in Milan.

The earliest mention of pellagra in France dates from 1829, when Hameau published an account of cases observed since 1818 around Teste-de-Buche and in the plain of Arcachon.

In Rumania the first recognition of the disease is assigned to the year 1836; in Corfu, to 1839.

We know nothing of the history of pellagra in Egypt prior to the publication of Pruner's "Topographie Médicale du Caire," in 1847. Sandwith has shown that the disease is very prevalent in Lower Egypt, and also, though to a less extent, in Upper Egypt.

In the United States of America, although there is evidence of its sporadic occurrence there for a considerable time—at least fifty years—before its nature was recognized, pellagra was first diagnosed as such in 1907. It is prevalent especially in the south-eastern States. Dr. H. F. Harris, Health Officer of the Georgia State Board of Health, estimated that there were 50,000 cases of pellagra in his State, and in 1916 it was estimated that there were 150,000 pellagrins in the southern United States alone.

Etiology. *Sex.*—Both sexes are liable, but in different places the disease exhibits a very different predilection for the one or other sex in accordance with the occupations and habits of the people. In the United States it is said to be more prevalent in women from 17 to 40 years of age; the debilitating effects of menstruation, pregnancy, and lactation are held to be predisposing and determining factors.

Age.—Hitherto pellagra was considered to be a disease of middle age, the majority of cases occurring between 20 and 50. Sambon has shown that within the endemic centres children are attacked, and that no age is exempt, he having seen the characteristic symptoms in a woman over 100 years old and in infants of barely 3 months.

Occupation. — The disease is most prevalent among field-labourers. The inhabitants of towns, even of those in the very heart of intensely pellagrous districts, enjoy an immunity similar to that of town-inhabitants as regards malaria. Felix points out that pellagra is quite exceptional among the Jews, who, as a race, rarely engage in agriculture. Bouchard says that herdsmen in pellagra regions are exempt. Pellagra occurs most frequently in

Digitized by Google

rural labourers living from hand to mouth, and seldom attacks people in good circumstances. This has long been recognized in Italy, and the figures given by Gruner for the southern States of the United States—258 cases had lived in poverty, 59 in comfort, 6 in affluence—show that the same remark applies to America.

Season.—Of all diseases with marked seasonal connection, pellagra is one of the most striking. As in the case of malaria, the pellagra season varies in different localities, but is always the same in the same locality.

In Europe the disease invariably appears in manifest and epidemic form during the spring and autumn quarters of the year, the spring outbreak being by far the more severe, the autumnal recurrence often inconspicuous or lacking. In Egypt, according to Chalmers, there is a spring invasion occurring in the months of April and May, and an autumn recurrence in November. In Nyasaland, according to Stannus, pellagra seems to prevail chiefly during August, September, and October, which are the spring months in the southern hemisphere, and again, though to a less extent, in January, February, and March (fall recurrence). In the United States of America, owing to the vast extent of territory and great variety of climates, the periodical incidence of the disease is necessarily different in different sections. In the northern States, as in Europe, the disease exhibits the usual well-marked double incidence, the spring outbreak occurring in May and June, the autumnal one in September and October. In the far south the disease may appear as early as January, and may be met with at any period of the year. In Barbadoes the disease seems to prevail more or less from May to October or November. Whilst the wide range of pellagra throughout the world might lead one to believe that climate exerts no special influence, the very definite seasonal periodicity of the disease shows that climatic factors play an important, though indirect, part in its etiology.

Epidemiology.—An important epidemiological feature of pellagra, in addition to those already mentioned, is the marked fluctuation of its prevalence from year to year. Then there may be long periods of quiescence, followed by years of considerable activity during which the disease may be looked upon as a new invasion. Pellagra is in no way contagious. The sound may associate with the sick and remain healthy. Doctors, nurses, and attendants on pellagrins are not known to contract the disease. Pellagrous wet-nurses do not infect their charges, and attempts to transmit the disease by inoculation have failed.

Associated diseases such as ankylostomiasis, schistosomiasis, tuberculosis, sprue, dysentery, and syphilis play a very important part in favouring the development of pellagra, in accelerating its course, in modifying and aggravating its symptoms, and in determining its mode of termination.

The virus.—Pellagra has been ascribed to the most varied

Digitized by Google

causes, such as insolation, poverty, insanitary dwellings, syphilis, irritant oils, bad water, alcohol, garlic, onions, maize. Some have regarded it as "sunstroke of the skin," and D'Oleggio, in 1784, proposed that it should be called "vernal insolation." "Sun disease" was an old popular name, and certainly the skin manifestations of pellagra are influenced by the action of the direct rays of the sun. This was proved experimentally, first by Gherardini, who varied the limits of the eruption by systematically displacing parts of the clothing; and later by Hameau, who obtained differently shaped patches of erythema by means of gloves fenestrated in different ways. In smallpox and also in other exanthemata we notice a decided influence of light, more particularly of the actinic rays, on the production of their skin eruptions. Although light may influence the eruption in pellagra, this is no adequate reason for concluding that insolation is the cause of the disease, any more than that it is the cause of smallpox. In support of the sunlight hypothesis, certain experiments on the effect of sunlight on animals fed on a too restricted (unphysiological) diet have been advanced recently; but it is evident that this cannot be the whole though it may be part of the truth.

It would be idle to discuss the arguments brought forward to show that pellagra is caused by bad water, insanitary dwellings, poverty, syphilis, leprosy, rancid oil, sour milk, acid wine, bad cheese, rye, millet, buckwheat, common salt, onions, or garlic. The maize, or rather the protein-deficiency theory, on the other hand, demands a searching scrutiny.

Three main theories have been advanced for the causation of pellagra, and the evidence in favour of each of them must be categorically stated. These theories may be termed—(1) the intoxication theory, (2) the infection theory, (3) the food-deficiency theory.

1. *The intoxication theory.*—The general opinion is that pellagra appeared soon after the introduction of maize into Europe, and that it advanced *pari passu* with the extension of maize cultivation and with the more general adoption of the new cereal as an article of food. For these and other reasons maize is still held by many to be the causative agent of pellagra, just as a condition of rye is known to be the cause of ergotism; and, as in the latter case, various theories have been propounded to explain the operation of the assumed cause.

Lombroso and Bellardini, in 1871, first advanced the theory that the prevalence of pellagra in Italy was due to the consumption of diseased maize, and their ideas subsequently formed the basis for public measures against the disease in that country, as well as in

Digitized by Google

Southern Europe. A large amount of work has been done upon the saprophytes acting on the grain. Maize may be damaged through damp or through being insufficiently cured, and in that state acts as a medium for the growth of poisonous fungi of different varieties, such as yeasts and moulds—*Penicillium glaucum*, *Mucor racemosus*, *Aspergillus niger*, and *A. fumigatus*. Lombroso claimed to have produced pellagrous symptoms in fowls by injection of alcoholic and watery extracts of damaged grain, but experiments made on the same lines since that date can in nowise be considered conclusive.

While it is certainly true that pellagra occurs commonly in those countries in which maize flour enters largely into the composition of bread, in this manner forming the staple article of diet, yet it is difficult on this basis to account satisfactorily for the sporadic cases of this disease which have been reported from the British Isles, Germany, Poland, China, and Nyasaland, where maize does not enter the dietary at all.

That pellagra is due to poisons elaborated from maize *within the alimentary canal* is disposed of by the harmlessness of this cereal in non-pellagrous districts.

2. *The infection theory.*—Pellagra has been considered to be a septicæmia due to various organisms, as for instance *Aspergillus fumigatus* (Ceni), while Tizzoni described a streptobacillus in the blood and fæces. Neither of these claims has secured any adequate support

Sambon since 1905 has been the staunch antagonist of the maize or "*zeist*" theory. On epidemiological grounds he has maintained that pellagra is a protozoal disease, and points to midges of the genus *Simulium* as being the probable transmitters of the hypothetical parasite. It cannot be said that this hypothesis has received much support; there are districts, as, for instance, Barbadoes, where pellagra is rife, but where these insects do not exist, or to a very limited extent only, and the Thompson-McFadden Commission has pointed out that the same conditions hold good in South Carolina. It has been a matter of comment that, if the disease were in any way insect-borne, cases would have occurred among British troops in the Near East during the late war, in countries such as Egypt and Palestine, in which pellagra was rife among the inhabitants, Turkish troops, and Armenian refugees, with whom British soldiers were so closely associated; but this has not been the case. There are ample observations which point to the absence of pellagra among nurses and attendants upon pellagrins in Italy and the United States.

Digitized by Google

No satisfactory evidence has yet been adduced that pellagra can in any sense be considered a directly infectious disease. Goldberger's carefully conducted experiments in 1917 would seem to dispose of this view entirely.

Goldberger obtained sixteen volunteers who, under his direction, attempted to infect themselves by ingesting skin scales, nasopharyngeal secretions, and epidermal excretions, over a period of six months. During this trying period they were, and subsequently remained, quite healthy.

3. *The food-deficiency theory.*—The first suggestion that pellagra is a disease produced by a deficiency in diet was made by Funk in 1913. Many observers now believe that pellagra, together with beriberi and scurvy, belongs to the "food-deficiency" diseases and is due to lack of certain vitamines in the food. The experiments conducted by Goldberger and Wheeler in America are the most telling in favour of such a hypothesis yet published.

In 1914 they fed a squad of eleven prisoners on a rich carbohydrate diet deficient in proteins. After five months, six of the number developed cutaneous symptoms suggestive of pellagra (the first lesions consisted of an erythematous patch on the scrotum). A second experiment in the converse direction also proved successful, for, by substituting a rich protein diet for one consisting in great part of carbohydrates, they succeeded in banishing pellagra from an orphanage asylum in which up to that time the disease had been in evidence.

There are those who think that preserved and tinned food may conduce, by the destruction of the vitamines in the process of conservation, to pellagra. A certain amount of evidence in favour of this view has been obtained in the southern United States.

The results of the Commission which investigated the prevalence of pellagra among the Turkish prisoners in Egypt tended to show that the error of metabolism in the disease is manifested in a primary deficiency of "biological proteins." Wilson and Roaf, members of the Commission, suggest that pellagra may develop in a susceptible subject, whose protein assimilation is sufficient for all needs while at rest, when bodily needs are increased by physical labour, or in one whose powers of metabolism have been vitiated by damage to the powers of alimentary absorption, as, for instance, by bacillary dysentery or other intestinal disease; in these cases a considerable loss of protein-absorption power was noted, the power being reduced to less than 67 per cent. It was noted, further, that as long as the prisoners were at rest pellagra was in abeyance, but broke out immediately they were subjected to any exertion. It would appear from these observations that in an individual whose balance of protein metabolism

Digitized by Google

has been undermined for a sufficiently long period, subsequent feeding with a suitable dietary may not prevent the appearance of pellagrous symptoms.

The assessment of the biological value of proteins in various articles of diet has brought out the interesting fact that maize is particularly deficient in this respect. Thus, the most recent developments in the study of pellagra are bringing the food-deficiency theory and the original " maize theory " of Lombroso into line.

The protein of maize flour, *zein*, is deficient in certain amino-acids, tryptophane and lysine, essential constituents of all proteins of proved biological value and known to be essential for nutrition. Millet and many other cereals contain a greater proportion of protein of biological value, and, if this be the case, a plausible explanation is obtained of the rarity of pellagra in Upper Egypt and the Sudan, where millet forms the staple article of diet, and the prevalence of the disease in the Delta, where maize is largely consumed.

A protein deficiency need not be peculiar to a maize dietary, and in this manner it is possible to account for the sporadic distribution of pellagra in countries in which maize is not consumed.

Biological protein value.—The amount of gross protein in a diet affords an unsatisfactory basis of comparison in that the vegetable protein is much less suitable for assimilation than that derived from animal sources. It has been found that only certain amino-acids contain nitrogen in a form which can be utilized for rebuilding tissues. From a consideration of these facts the term " biological value of protein " has been derived. The smallest amount of meat protecting a man of 70 kilos from a loss of body protein is 30 grm. per diem, of bread 76 grm., and of maize 102 grm. Wilson has suggested, as minimal amounts per diem, a biological protein value of 45 grm. (a figure representing a gross protein value of 120 grm. per diem) for heavy labour, and 40 grm. for light labour. A diet containing 80 grm. per diem gross protein value and less than 33 grm. biological protein value would seem to predispose towards the development of pellagra, as in the case of the Turkish prisoners already referred to.

The following is a table compiled by the Medical Research Committee of the " biological values " of various proteins, as measured by the relative " tissue-repairing " values of equal weights :—

Ox-meat	104	Caseinogen	70
Cow's milk	100	Peas	56
Fish	95	Wheat flour	40
Rice	88	Maize meal	30
Potato	79		

Digitized by Google

Alterations in the protein metabolism of the human economy may exert an influence upon the secretions of the ductless glands. Recent work by McCarrison and Rondoni upon the suprarenal glands during protein starvation indicates that the activity of these organs is thereby increased. It is conceivable that disturbances in the composition or amount of suprarenal secretion may determine the peculiar eruption of pellagra. For instance, in Egypt the Editor found the most constant lesion in pellagra autopsies was the condition of the suprarenals, which as a rule were atrophied and showed degenerative changes; occasionally they were the seat of extensive hæmorrhages.

The effects of feeding monkeys upon a diet deficient in biological proteins, and the emaciation and hyperæmia of exposed parts which result, suggest that it is upon these lines that the problem of pellagra may be solved ultimately.

It cannot be truthfully said that the protein-deficiency theory is yet proved. In face of some disquieting instances these views may require revision. One such occurrence has come under the Editor's personal observation, and has been reported by Enright in the *Lancet*, May 8th, 1920:

> In January, 1919, a certain number of German prisoners in Egypt, who up to that date had remained healthy, developed acute symptoms of pellagra, although, according to their own statements, they had always received an ample protein dietary, both before their capture in Syria and during their four months of captivity in Egypt. So far no extensive outbreak of pellagra amongst the half-starved masses of Central Europe consequent upon the War has been recorded.

Symptoms.—The course of pellagra is generally a long one. As noted by Strambio, the disease does not pursue any regular course, but one of repeated exacerbations and periods of quiescence. The initial symptoms are composed of mingled psychical and digestive disturbances. It is possible that these may recur for years without the appearance of skin eruptions. The patient is pale, has a peculiar staring look, and complains of headache, giddiness, and vague but often severe pains in the back and joints. His character changes; he becomes irritable, and at the same time stupid and morose.

At times the tongue is coated; later it loses its epithelium, the denudation extending not infrequently to the palate and gullet, and giving rise to a sore condition, often accompanied by a saltish taste and copious salivation. Associated with it is a leucoplakia at the angles of the mouth. The gums may be swollen and bleed easily, a condition which gave rise to the name "Alpine scurvy."

Digitized by Google

There may be eructations of gas, nausea, and vomiting. The appetite is variable. The epigastric region, and sometimes the lower part of the abdomen, are tense and painful. Constipation may be present, but in many instances there is diarrhœa of pale fermenting stools resembling those of sprue.

The skin symptoms.—Most observers regard the skin lesions of pellagra as the earliest manifestation of the disease, but possibly they are symptomatic of some chronic and deep-seated disturbance. At first an erythema, not unlike a severe sunburn, is observable on those parts of the body which are, as a rule, unclothed and exposed to the sun. (Plates XV., XVI.) The eruption is symmetrical and characteristic. It appears suddenly, first on the back of the hands and feet, then on the forearms, legs, chest, neck, face, and, it may be, on the scrotum, or on the female genitalia. The patches of erythema are irregular in outline and intensity. Very characteristic are the symmetrical patches behind the mastoid processes, a ring or collar round the neck, and a butterfly patch over the bridge of the nose resembling lupus erythematosus. The affected area is swollen and tense, and the seat of burning or itching sensations which become particularly acute on exposure to the sun. The character of the eruption is well shown in the Plates. In this case it is limited by the outline of the Turkish slippers the patient wore. The congestion disappears completely, but temporarily, on pressure. Petechiæ are common on the affected parts, and blebs with clear, opaque, or blood-stained contents of feebly alkaline reaction may form. The eruption usually lasts about a fortnight, and is followed by desquamation, which leaves the skin rough, thickened, and permanently stained of a light sepia colour. This is especially marked on the back of the hands and on the elbows, and forms recognizable evidences of the disease. It is on account of this roughness of the affected skin that the disease is called "pellagra," an Italian word meaning rough skin. An obstruction to the sebaceous ducts on the alæ nasi produces a peculiar sulphur-flaked appearance of the skin in that region.

Implication of the *nervous system* is indicated by tremor of the tongue, exaggerated deep reflexes, and mid-dorsal spinal tenderness. The patient suffers from obstinate sleeplessness, occasionally from uncontrollable sleepiness. He experiences great weakness, especially in the lower extremities, and is subject to peculiar attacks of giddiness, with a tendency to fall forwards or backwards. Another characteristic symptom is a feeling of burning in the palms of the hands and the soles of the feet. "Chvostek's

Digitized by Google

1

2

3

Fig. 1.—Characteristic inflamed tongue of acute pellagra.
Fig. 2.—Early pellagrous rash, with cellular infiltration and pigmentation.
Fig. 3.—Typical pellagrous rash over occiput and mastoid processes, with formation of "rosary" round the neck.

PELLAGRA.

By permission of Dr. J. I. Enright.)

PLATE XV.

Digitized by Google

Digitized by Google

sign," mechanical irritability of the facial nerve, is said to be present in the majority of cases.

After the disappearance of the eruption, atrophic patches of skin remain in the interdigital clefts, which, together with muscular wasting, give the appearance of washerwoman's fingers. The hands, in fact, are aged out of proportion to the rest of the body. The nails become atrophied and brittle.

As a rule there is no marked permanent elevation of temperature, but periods of slight fever occur at irregular intervals.

Two or three months after onset the symptoms abate and, although the affected skin areas remain dark-coloured and rough, the disease appears to be arrested. Next spring, however, the whole series of phenomena recurs in a more severe form. The eruption assumes a darker colour. The depression of spirits deepens into melancholia, which may have maniacal interludes, with a peculiar tendency to suicide, especially by drowning. The general feeling of weakness increases; the patient loses weight and is unable to work; his gait becomes uncertain and somewhat of the spastic paraplegic type. The tongue becomes tremulous. The pains in the head and back become very acute, and there may be lightning pains, cramps, twitchings, tremors, and even epileptiform seizures of the cortical variety. Diarrhœa may now be troublesome.

For several years the disease may thus recur in the spring with increasing severity. The patient becomes greatly emaciated, paralytic, and completely demented. Helpless, bedridden, suffering from incontinence of urine and uncontrollable diarrhœa, covered with bedsores, and neglected, he dies from exhaustion or from some intercurrent disease.

The duration of pellagra is exceedingly variable. It may last only two or three years; it usually extends to ten, fifteen, or more.

In a proportion of cases, more especially if the patient leaves the endemic area and comes under favourable hygienic influences early in the disease, recovery may take place.

Cases differ considerably. In some the nervous symptoms predominate, in others the gastro-intestinal, in others again the cutaneous. Forms of hyperæsthesia may occur in different regions of the body. Ocular symptoms, such as ptosis, hemeralopia, diplopia, amblyopia, mydriasis, are not uncommon. The urine is generally alkaline and may rapidly become ammoniacal. It may also contain tube-casts and traces of albumen and, usually, indican. The erythrocytes and hæmoglobin are diminished to a limited extent in

Digitized by Google

the uncomplicated disease. As a rule there is a definite lymphocytosis, but it cannot be said that, although usually disturbed, the differential leucocyte count is constant or characteristic. The gastric juice is deficient in hydrochloric acid.

A very acute form has been described under the name of "pellagra typhus." In this there are intense prostration, high temperature, muttering delirium, pronounced nervous tremor, generalized rigidity, and convulsions. In extensive outbreaks of pellagra, such as occurred among the Turks during the War, cases of this description may be comparatively common.

It has been estimated that in Italy from 4 to 10 per cent. of the pellagrins become permanently insane. Similarly, in the United States of America the pellagrins are becoming a notable feature in the lunatic asylums. The type of insanity is usually a most profound melancholia with a suicidal tendency; one has seen cases resembling in their clinical features general paralysis of the insane.

Morbid anatomy.—The pathological characteristics essential to pellagra are usually obscured by complicating diseases, such as bacillary dysentery and tuberculosis.

A constant and striking feature is the great emaciation. The viscera show chronic degenerative changes, particularly fatty degeneration and a characteristic deep pigmentation. The intestinal walls are greatly attenuated through wasting of their muscular coat, while at the same time the mucous lining is hyperæmic and, not infrequently, ulcerated. The liver and spleen are usually atrophied. The suprarenal capsules may be larger than normal, and the cortex may be black, while the medulla is whitish in colour, but it may be the seat of hæmorrhages.

There may be actual wasting of the brain, the ventricles being distended by an excess of fluid. In the cord the lateral columns and the crossed pyramidal tract are especially implicated, but the direct cerebellar tracts usually escape. The anterior cornual cells are frequently atrophied and deeply pigmented. The posterior columns do not escape, the median portion being often degenerated. The degenerative changes in the lateral columns are chiefly in the middle and lower third of the dorsal region, those of the posterior columns principally in the cervical and upper dorsal region. The cerebro-spinal fluid shows little change; there is usually no increase in the globulins.

Mott has given a detailed account of the histological changes in the nervous systems of two cases of pellagra—one of English, the other of Egyptian origin. He remarks as to the changes in the

Digitized by Google

Photo: Dr. A. D. Bigland.

PELLAGRA RASH ON FEET.

The dorsa of the feet had been exposed to the sun in the area between the turned-up trousers and the uppers of the shoes.

PLATE XVI.

Digitized by Google

Digitized by Google

cerebrum, cerebellum, pons, medulla, and spinal cord, that in none of the sections was there any evidence of meningeal or perivascular infiltration with lymphocytes, plasma cells, or polymorphonuclear leucocytes. This absence of chronic meningo-encephalitis, a chronic inflammatory condition so characteristic of certain protozoal diseases, contraindicates the protozoal theory of pellagra, although it cannot be said to disprove it, for in malaria the vessels may be crowded with parasites and yet no perivascular or meningeal reaction be detectable. Moreover, although all the changes were like those produced by a chronic toxæmia, the cause of that toxæmia had not been demonstrated. All the posterior spinal ganglia cells showed, in varying degree, a pronounced chromatolysis, swelling of cells, and disappearance of Nissl's granules, and all the anterior horn cells and their homologues in the medulla and pons a varying degree of perinuclear chromatolysis. There was marked chromatolysis of the cells of Clarke's columns. The Betz cells of the cortex and the cells of Purkinje showed similar changes, but in a less degree. Recently, Roaf has noted peculiar degenerative changes in the abdominal sympathetic ganglia.

Diagnosis.—Of course, doubtful cases are occasionally encountered, but a localized erythema associated with nervous symptoms, particularly mental symptoms, great debility, and seasonal recurrence, in a person in or coming from a pellagrous district, can hardly be confounded with any other disease. The rash may be mistaken for acrodynia, erythema, eczema solare, trade dermatitis, lupus erythematosus, or syphilis; the gastro-intestinal disturbance and the glossitis for sprue; while the nervous manifestations have to be differentiated from hysteria, general paralysis of the insane, ergotism, and lathyrism.

Treatment.—Arsenic in large doses is now regarded as a drug of value in the treatment of pellagra. Fowler's solution by mouth—5 drops two or three times daily, increased by 1 drop daily until evidences of a toxic nature are induced—or hypodermically in combination with carbonate of soda (3 to 5 gr.) two or three times a week, is said to be productive of good results if given early in the disease, and, of course, combined with good hygienic conditions and removal from the endemic area. Atoxyl, soamin, and salvarsan have also been commended. No case should be regarded as cured until the patient has been absolutely free from all symptoms for at least two years.

In early stages remarkable improvement is noted with a dietary rich in protein, such as meat and eggs, although in the advanced stages this is useless, and the disease may be regarded as incurable.

Digitized by Google

In Italy the Government, basing its action on the maize theory of pellagra, has provided grain-drying appliances for bakeries, and other hygienic advantages, including better house accommodation, also special asylums (*pellagrosari*) for the treatment of the disease in its earlier stages. It is stated that a decrease of the malady has followed these measures. Nevertheless, pellagra seems to have increased of late years, especially round Perugia and in other districts of northern Italy in which these measures have been most strictly carried out.

As there has been no instance of a nurse or attendant in any of the lunatic asylums of the United States acquiring the disease, it is evident that pellagra is not a directly communicable disease, and that therefore any apprehension on this account is unwarranted.

Digitized by Google

CHAPTER XXVII

SCURVY IN THE TROPICS

ALTHOUGH scurvy is associated in the popular mind with Arctic exploration and prolonged sea-voyages, it is nevertheless comparatively frequent in tropical natives when, owing to famine or other causes, the inhabitants are deprived of their accustomed diet. It was a common disease during the War, in the Turkish army, among Indian troops in Mesopotamia and East African porters, and has long been known on the South African mines as "Rand scurvy." In this variety the spongy gums and loose teeth, so familiar in the classical type of the disease, are not seen, but the heart undergoes hypertrophy and subsequently dilatation, added to which are neuritic symptoms suggestive of beriberi, but the knee-jerks are invariably exaggerated. Epidemics of this disease are apt to occur amongst gangs of coolies and labourers who are fed on an unsuitable dietary; this is especially the case in natives recruited for labour purposes and fed upon dried cereals and preserved foods, who previously had been in the habit, in their own villages, of consuming large quantities of fresh vegetables and fruit such as bananas.

Etiology. — Scurvy is now generally regarded as a food-deficiency disease. It is produced not by general starvation but by the absence of an accessory factor, or vitamine, in the food. This body (p. 352) is present in all fresh vegetables, swedes, turnips, onions, and fruit, especially the orange and lemon. It is very sensitive to prolonged heat and drying, and therefore is absent from tinned fruits and vegetables, and from dried legumes such as peas and beans, but reappears directly these seeds are induced to germinate. Yeast, fresh meat, and milk contain only small quantities of the antiscorbutic vitamine, and, curious to relate, according to Chick and Hume, preserved *lime*-juice little or none at all, while preserved lemon-juice is rich in this substance.

The antiscorbutic factor is soluble in water and in alcohol, and will pass through dialysing parchment, or a porcelain filter, without appreciable loss. It is more stable in acid than in alkaline media.

Symptoms.—The onset of scurvy is insidious, with loss of weight, progressive weakness and pallor, and a feeling of stiffness

Digitized by Google

in the leg muscles. The gums soon become affected with a swelling and sponginess of the alveolar margin. As the disease progresses the gums present fungating masses projecting beyond the teeth, which loosen and fall out. The tongue swells, the salivary and lymphatic glands enlarge, and the breath becomes very foul. The skin becomes dry and rough, and very soon subcutaneous petechiæ form on the limbs and trunk, commencing *round the hair-follicles*, especially on the thigh. Hæmorrhages occur into the muscles of the thigh and into the knee-joint. Very painful effusions under the periosteum form irregular nodes, which may break down and ulcerate. Œdema of the ankles is common, and hæmoptysis or hæmatemesis may occur. Any injury is apt to cause a hæmorrhage.

Together with these objective symptoms the patient experiences cardiac distress, with irregularity of the pulse-beat and the appearance of hæmic bruits at the apex. The urine is generally loaded with albumen. On the other hand, the digestive system is not disturbed, constipation being more constant than diarrhœa. The physical disturbances are pronounced. Headache is noted early, and delirium supervenes in the later stages. In the most advanced cases the jaw-bones generally become necrotic.

In the young the formation of a "scurvy rosary" at the junction of the costal cartilages and separation of the epiphyses of the long bones may occur.

Diagnosis.—To diagnose scurvy under modern conditions is not a difficult matter. But care must be taken to distinguish mild cases from pyorrhœa alveolaris.

Treatment is chiefly dietetic. The disease, if recognized early, readily yields to a diet composed of fresh fruit and vegetables; when these are unprocurable, fresh meat can be substituted, but is by no means so satisfactory. Germinating peas are useful when fresh vegetables are unobtainable. The following method of using peas and other pulses is recommended by Chick and Hume:—

SUGGESTED METHODS OF PREPARING PEAS, LENTILS, OR OTHER PULSES FOR THE PREVENTION OF SCURVY, IN THE ABSENCE OF FRESH VEGETABLES

1. The dry seeds must be whole, retaining the original seed-coat, and not milled or decorticated.

2. They must be soaked in water for several hours; the time necessary depends on the temperature—24 hours at 50° to 60° F., and 12 hours or less at 90° F.

3. The water must then be drained away and the peas, etc., allowed to remain in the moist condition with access of air. They will then germinate and the small rootlet grow out. . . . This germination will take 48 hours at 50° to 60° F., and 12 to 24 hours at 80° F.

Digitized by Google

Soaking.—The peas or other pulses, placed in a *clean* sack, should be steeped in a trough, barrel, or other suitable vessel, full of clean water, and should be occasionally stirred. The sack and trough, etc., should be large enough to allow for the swelling of the peas to about three times their original size. In a hot climate 6 to 12 hours should suffice for this soaking.

Germination.—The peas should be lifted out of the water and spread out to a *depth not exceeding 2 to 3 inches* in a trough or other vessel with sides and bottom porous or well perforated with holes. This is to allow *complete* access of air. *The seeds must be kept in a moist atmosphere.* This is done by covering with damp cloth or sacking, which is sprinkled (by hand or automatically) as often as is required to keep the peas thoroughly moist underneath. . . . *All the vessels should be clean.*

4. *It is important that the germinated pulses should be cooked and eaten as soon as possible after germination, and should not be allowed to become dry again ;* in that case the antiscorbutic properties acquired during the process of germination will again be destroyed. The pulses should not be cooked longer than necessary.

Raw onions are very valuable antiscorbutics, and raw potatoes and swedes have a very definite curative value. Canned vegetables, with the exception of canned tomatoes, are useless.

For native troops, Kaffir beer made from germinating grain is said to be of great value.

Prophylaxis is obvious, and consists in following the directions laid down, together with attention to oral hygiene. Vegetables must not be overcooked, and wherever possible, in mines or tropical camps, native gardens should be established. Men threatened with scurvy should be given light work only.

Digitized by Google

Section III.--ABDOMINAL DISEASES

CHAPTER XXVIII

CHOLERA

Definition.—An acute, infectious, epidemic disease, characterized by profuse purging and vomiting of a colourless serous material, muscular cramps, suppression of urine, algidity and collapse, the presence of a special bacterium in the intestine and intestinal discharges, and a high mortality.

History and geographical distribution.—It is probable that from remotest antiquity cholera has been endemic in Lower Bengal, and that thence, from time to time, it has spread as an epidemic over the rest of India. European physicians observed it there in the sixteenth, seventeenth, and eighteenth centuries, but it was not until the great epidemic extension of 1817 that the disease seriously attracted the attention of the profession in Europe. In that year cholera began to spread all over Asia, extending eastwards as far as Pekin and Japan, southwards to Mauritius, and westwards to Syria and the eastern shores of the Caspian. Stopping short at Astrakhan in 1825, it did not on that occasion invade Europe. It is probable that other Eastern towns —Bangkok, Canton, and Shanghai, for example—are also foci of endemic cholera ; in fact, it may be said that the disease is lurking in almost every insanitary Eastern town where " cholera carriers " abound.

European epidemics.—In 1830 cholera visited Europe for the first time. Advancing through Afghanistan and Persia, it entered by way of Russia, and swept as an epidemic over nearly the entire Continent, reaching Britain at the beginning of 1832. During the same summer it crossed the Atlantic to Canada and the United States. This epidemic did not die out in Europe till 1839. Since that time there have been at least five European epidemics—1848–51, 1851–55, 1865–74, 1884–86, and 1892–95. Minor epidemics have occurred in Europe since, but they have been restricted in area. During the Balkan War of 1913, and in the course of the Great War, especially in the Balkans and in Mesopotamia, there were many outbreaks of cholera, but the

Digitized by Google

disease did not extend as an epidemic beyond the actual seat of war.

Great Britain has been seriously involved in four only of these epidemics—namely, in 1832, 1848, 1854–55, and in 1866. On the occasion of the last two European epidemics, although the disease was frequently imported, it did not spread in Britain. America has not been so fortunate, for, although the 1870–3 epidemic practically spared Great Britain, it crossed the Atlantic and, entering by way of Jamaica and New Orleans, raged for a time in the United States.

From a study of the march of these various epidemics it is to be concluded that cholera reaches Europe by three distinct routes—(1) via Afghanistan, Persia, the Caspian Sea, and the Volga valley; (2) via the Persian Gulf, Syria, Asia Minor, Turkey in Europe, and the Mediterranean; (3) via the Red Sea, Egypt, and the Mediterranean.

With certain exceptions, hereafter to be mentioned, there is hardly an important country in the world which has not, at one time or another, been visited by cholera in the course of some of its pandemic extensions.

Etiology. *The disease is carried by man.*—A study of the various epidemics shows that in its spread cholera follows the great routes of human intercourse, and that it is conveyed chiefly by man—probably in its principal extensions by man alone—from place to place. In Britain and the United States, for example, the places first attacked have been invariably seaports in direct and active communication with other ports already infected. In India, although the problem is much more difficult to unravel, in certain instances the influence of human intercourse in diffusing the disease can be distinctly traced. Thus the extensive pilgrimages, so frequent in that country, are a fruitful source of its rapid spread. During these gatherings hundreds of thousands of human beings are collected together under highly insanitary conditions—as at the Hurdwar and Mecca pilgrimages. Cholera breaks out among the devotees, who, when they separate, carry the disease along with them as they proceed towards their homes, infecting the people of places they pass through. Cholera never travels faster than a man can travel; but in modern times, owing to the increased speed of locomotion and the increased amount of travel, epidemics advance more rapidly and pursue a more erratic course than they did sixty years ago.

Isolation secures immunity.—In the case of isolated countries the absence of active and frequent intercourse with the outer

Digitized by Google

world favours immunity; thus, though so near to the reputed home of cholera, the Andaman Islands have never been visited by that disease. Similarly, Australia and New Zealand hitherto have enjoyed practical exemption. The same can be said of the Pacific Islands, the Cape of Good Hope, the West Coast of Africa, Orkney and Shetland, Iceland, the Faroe Islands, and many of the islands of the Atlantic.

Local conditions favouring the presence of cholera.—On the whole, it may be said that low-lying districts, particularly those along river banks, are more subject to the disease than high and dry situations; and that overcrowding and unhygienic conditions generally conduce to its prevalence. The principal and special element, however, which determines the diffusion of cholera is, undoubtedly, the character of the water supply.

Cholera in the main a water-borne disease, entering by the stomach.—The earliest and still one of the most telling pieces of evidence in favour of the water-borne theory of the diffusion of cholera we owe to the late Dr. Snow. In August, 1854, cholera was epidemic in parts of London, notably in the neighbourhood of Golden Square, Soho. A child, after an illness of three or four days, died of the disease at 40, Broad Street, on the 2nd of September. The discharges from the patient had been thrown into a leaky cesspool which, as was subsequently discovered, drained into a well only three feet away. This well supplied the neighbourhood with drinking-water. On the night of the 31st of August cholera broke out among those who used the water of this particular well, very few escaping an attack. On the 2nd of September a lady died of cholera at Hampstead; this proved to be the first case in the district, and on inquiry it was found that she had been habitually supplied with drinking-water from the Broad Street well referred to, as she had formerly resided in Broad Street, and had retained a liking for the water from this particular well. She drank some of the water which had been procured on the 31st of August, both on that day and again on the 1st of September. On the latter day she was seized with cholera. A niece, on a visit to this lady, also drank some of the same water; she, too, was attacked by cholera, and died. A servant also drank the water; although she suffered to some extent, she recovered. So far as could be ascertained by careful inquiry, these people had had no connection whatever with the cholera district except through the water fetched from this particular Broad Street well.

Another remarkable illustration of the diffusion of the cholera germ by water is supplied by an epidemic in Hamburg. At the

Digitized by Google

time the sanitary conditions under which the inhabitants of the contiguous cities of Hamburg, Altona, and Wandsbeck lived were practically identical, save in the matter of water supply. Hamburg and Altona both drew their water from the Elbe; but, whereas the water distributed to the people of Altona was most carefully filtered, that supplied to the people of Hamburg was simply pumped up from the river and passed directly into the mains without filtration or purification of any description. The Wandsbeck water came from a lake, and was filtered. In Hamburg, during the epidemic, there were 8,605 deaths from cholera, equal to 13·4 per thousand; whereas in Altona only 328 deaths occurred, equal to 2·1 per thousand. The death-rate in Wandsbeck was similar to that of Altona. Hamburg and Altona are contiguous, and practically one city. At one part a street forms the boundary between the municipalities. On one side of this street, the Hamburg side, there were numerous cases of cholera; on the Altona side there were no cases. The houses on both sides of the street were of the same character and occupied by the same class of people. The only difference, so far as could be ascertained, was in the water supply: the houses on the healthy side of the street received Altona water; those on the cholera-stricken side Hamburg water. It was remarked that a certain group of houses on the Hamburg side remained free from the disease. On investigation it was found that, unlike the other houses on the same side, these houses derived their water supply from an Altona main.

These and many similar facts which might be adduced clearly point to water as a principal medium for the diffusion of the cholera germ.

The virus contained in the dejecta.—Evidence equally conclusive tends to show that the germ on being swallowed by man multiplies in his alimentary canal, and, on being voided in the dejecta, subsequently finds its way by a route more or less direct to water again, in which, under favourable conditions, it continues still further to multiply. An illustration, amounting almost to proof, of the fact that the germ of cholera is contained in the stools of cholera patients is supplied by Macnamara. Some of the characteristic rice-water discharge from a cholera patient got mixed accidentally with a few gallons of water. This was exposed to the sun for twelve hours. Early the following morning 19 persons each drank about an ounce of the mixture. Within thirty-six hours 5 of these 19 persons were seized with cholera.

Conditions of infection are complex.—It is evident that the ingestion of the germ is a necessary condition for the production

Digitized by Google

of the disease, but there are many facts which render it equally evident that this is not the only condition. Were it the only condition, then every one of those individuals referred to by Macnamara would have sickened. What the other necessary conditions may be it is, in the present state of knowledge, impossible to say.

There is reason to believe that not only are the conditions complicated as regards the susceptibility of the individual, but also that they are equally complex as regards the germ itself in relation to its pathogenic, proliferating, and diffusing properties.

Fig. 88.—Cholera bacillus. Agar culture: 24 hours' growth. × 1,000. (*Muir and Ritchie.*)

Discovery of the comma bacillus, spirillum, or vibrio.—The cholera vibrio was first discovered by Koch in Egypt in 1883; this discovery he confirmed in Calcutta in 1884 by finding it in every case of the disease he examined. His observations have since been abundantly confirmed. If only on account of its diagnostic value, the comma bacillus, therefore, is an organism of importance; but as many high authorities regard it as a necessary concomitant and even as the actual germ and true cause of Asiatic cholera, the vibrio acquires an importance of the first rank.

Description of the comma bacillus.—The comma bacillus (Fig. 88) is a very minute organism, 1·5 to 2 μ in length by 0·5 to 0·6 μ in diameter—about half the length and twice the thickness of the tubercle bacillus. It is generally slightly curved, like a comma;

Digitized by Google

hence its name. After appropriate staining, at each end, or at one end only, flagella can be distinguished—sometimes one, sometimes (though less frequently) two. These flagella, though of considerable length—from one to five times that of the body of the bacterium—owing to their extreme tenuity are difficult to see in ordinary preparations. They are not always present during the entire life of the parasite. In virtue of this appendage the bacillus exhibits very active spirillum-like movements. The individual bacilli when stained show darker parts at the ends or at the centre, suggesting spore formation. Sometimes in cultivations two or more bacilli are united, in which case an **S**-shaped body is the result; or it may happen that several bacilli are thus united, producing a spirillar appearance.

The comma bacillus is easily stained by watery solutions of fuchsin, or by Löffler's method, dried cover-glass films being used. It is decolorized by Gram.

The bacillus grows best in alkaline media at a temperature of from 30° to 40° C. Growth is arrested below 15° or above 42° C.; a temperature over 50° C. kills the bacillus. Meat broth, blood serum, nutrient gelatin, and potato are all suitable culture media. It multiplies rapidly without curdling in milk. It dies rapidly in distilled water; it survives longer if salt be added to the water—for instance, 285 days in sea-water.

In gelatin plates it grows readily as minute white colonies, irregular in shape, and granular, with surrounding liquefaction, into which the colonies of bacilli sink as into funnel-shaped depressions. In gelatin stab cultures the growth at first is most active near the surface; later, as growth proceeds along the needle track, a finger-shaped liquefaction results, which in time extends to the sides of the tube. In older cultures involution forms are common; they may die out after five or six weeks.

Agar is not liquefied, and in it the cultivations retain their vitality longer. On potato, at 20° to 30° C., the culture appears as a thin, brownish, porcelain-like film. In broth some of the bacilli form a scum on the surface; others, falling in masses to the bottom, leave the body of the liquid clear. As a rule, the cholera vibrio does not produce hæmolysis if blood be added to the medium it grows on, such as agar, after twenty-four hours' incubation. The test is best performed in a fluid medium by adding varying amounts, from 1 c.c. downwards, of a three days' culture in alkaline broth to 1 c.c. of a 5-per-cent. suspension of goat's corpuscles and then thoroughly mixing. After incubation for two hours the tubes are placed in the ice-chest overnight and read the

Digitized by Google

next day. With the solutions of sugars (1 per cent.) usually employed, the vibrio produces acid, without gas-formation, in glucose, mannite, saccharose, and maltose. The fermentation of lactose, with acid production, occurs two to three days later.

Although, taken together and in conjunction with the morphological appearances, these culture characters are fairly distinctive, nevertheless certain other vibrios, such as Finkler's spirillum, behave very similarly; and, as the morphology and behaviour of these paracholera organisms are very much like those of the cholera vibrio, a mistake is easily made. The cholera-red reaction is obtained by the addition of pure sulphuric acid to a culture in 1-per-cent. peptone solution. This reaction is always given by the true cholera vibrio, but is not distinctive of that organism, as atypical vibrios and certain strains of *B. coli* have been found to give a similar but less marked reaction. The reaction depends upon the fact that both indol and nitrite are formed by the spirillum in the medium, whereas in the case of other organisms it is necessary to add the former in order to obtain the necessary rosindol reaction.

The true Koch's vibrio may further be recognized by employing an artificial immune rabbit's serum, which will agglutinate the organism microscopically up to a titre of 1 : 12,000. This is the most satisfactory method of identifying the cultures, and is, in fact, the final test.

In careful and practised hands the diagnosis of cholera by the microscopic and cultural characters of the vibrio may be made with practical certainty.

Is the comma bacillus the germ of cholera?—Although it may be safely asserted that cholera is intimately associated with the comma bacillus, it does not necessarily follow that this organism is the cause of cholera. Many attempts have been and are being made to establish such a relationship. Nevertheless, what may be considered as absolute proof is still wanting—such proof as alone can be afforded by the production in man, or in the lower animals, of a disease in every respect like cholera by the administration of pure cultures of the comma bacillus. Short of this the proof may be said to be almost complete; indeed, by not a few the causal relationship of the bacillus to the disease is considered as established.

Since Koch first announced his discovery many facts having a bearing on the subject have been brought to light, some in favour of his views, some apparently militating against them.

1. It has been found that there are several bacilli with morphological and cultural characters closely resembling those of the

Digitized by Google

cholera comma; notably the Finkler-Prior bacillus of cholera nostras, allied organisms such as the El Tor, the paracholera inagglutinable vibrios, the organisms described by Metchnikoff in fowl cholera and by Deneke in decomposing cheese, comma-shaped bacilli discovered by Cunningham, and certain species found in river water. Koch and others maintain that, though morphologically similar, as these various bacilli behave so differently from that of cholera in culture media, they must be considered as biologically specifically distinct.

2. Cultures of pure bacilli have many times been swallowed by way of experiment; yet, although in some instances diarrhœa with comma bacilli in the stools has resulted, in only one instance —recorded by Örgel of Hamburg—has true cholera been produced. On this account it is held by some that the comma bacillus cannot be regarded as the germ of cholera. Against this it is advanced that other factors must be present to ensure the induction of cholera by such experiments; for example, a suitable and peculiar condition of the body, possibly, as Buchner suggests, some second and as yet unknown micro-organism. Buchner accordingly regards cholera as the result of a mixed infection. It is to be presumed, therefore, that, in the two or three instances in which cholera followed on the intentional or accidental ingestion of cultures of the cholera vibrio, these secondary but essential conditions were present. It must be remembered also, in assessing the value of negative feeding experiments, that the cholera vibrio, like other pathogenic bacteria, may, through cultivation or otherwise, lose its virulence while retaining its morphological and cultural qualities.

3. A few cases of what, from a clinical point of view, appears to be true cholera have been observed in which the most careful and prolonged bacteriological examinations failed to detect the comma bacillus. Therefore, it has been advanced, as cholera can occur without the comma bacillus, the comma bacillus cannot be the cause of cholera. Against this it has been said that these observations were defective; that although the bacillus was not found, it by no means follows that the bacillus was not present at some time in the case.

4. The comma bacillus has been observed in the stools of individuals who did not at the time or afterwards suffer from cholera. To this it is answered that although one of the necessary conditions for the production of cholera was present, others, equally necessary, were absent. Possibly, as Pettenkofer has remarked, for the production of an attack of cholera three things may be

Digitized by Google

necessary, X, Y, and Z. The comma bacillus may be the X, but in the absence of the Y, certain local, and of the Z, certain personal, conditions disease does not result.

5. It has been found impossible to produce true cholera in the lower animals by the administration of comma bacilli, or any condition with clinical symptoms closely resembling cholera. Koch and others, in certain experiments on guinea-pigs, acting on the supposition that the acid in the stomach killed the bacillus, neutralized this by the administration of sodium carbonate, and paralysed the intestine by intraperitoneal injections of tincture of opium. In this way they claim to have succeeded in killing guinea-pigs with symptoms to a certain extent like those of cholera. There are many sources of fallacy in this experiment, as has been pointed out by Klein and others. Exactly similar results can be got by using the Finkler-Prior and other bacilli. The most promising experiments in this direction are those by Jablotny on the ground-squirrel, *Spermophilus guttatus*. By administering to this animal comma cultures in alkaline media, a disease in many respects like cholera was produced; and, in the intestines and discharges of the animals experimented on, cholera-like pathological changes were found, as well as comma bacilli.

Toxins.—Filtered cultures of Koch's vibrio have little toxic action; the virus is apparently liberated by the disintegration of individual organisms. Dead cultures, when given by the mouth, produce no effect, unless the intestinal epithelium is injured. The toxic bodies are mostly destroyed at 60° C.; when ground up, and frozen by means of liquid air, an extract of high toxicity to laboratory animals, if injected intravenously, is obtained.

The cholera vibrio is a powerful tissue-irritant when injected hypodermically, and at the same time produces a smart febrile reaction. This fact, together with the rapid and intense prostration, which appears to be out of all proportion to the amount of catharsis present, suggests that the lethal effects of the vibrio are attributable not alone to the drain of fluid from the blood and tissues, but also to the absorption of a cholera toxin from the intestines. The modern tendency is to regard the clinical phenomena as the result partly of local irritation and partly of toxæmia.

Immunity.—The guinea-pig or rabbit may be easily immunized against the cholera vibrio by repeated intraperitoneal injections of killed cultures of the vibrio. The blood serum thus obtained shows marked agglutinative properties in a high titre towards cultures of the organism. Furthermore, this serum, when injected

Digitized by Google

into a non-immune animal, has marked protective power against even four or five times the lethal dose of organisms. When this happens, active bacteriolysis takes place, a phenomenon known as Pfeiffer's reaction. The test is performed as follows:—

A loopful of a young agar culture of the vibrio is added to 1 c.c. of bouillon containing 0·001 c.c. of anti-cholera serum, and is injected into the peritoneal cavity of a young guinea-pig; by means of capillary tubes inserted into the peritoneum the peritoneal fluid is examined microscopically every few minutes. If the original culture was a true Koch's vibrio, the organisms break up into globules; if not, no change takes place.

Symptoms.—An attack of cholera commences in one of two ways: either it may supervene in the course of what appears to be an ordinary case of diarrhœa, or it may come on suddenly and without any well-marked prodromal stage. During cholera epidemics diarrhœa is unusually prevalent. It is a common observation that at such times an attack of this latter nature, after a day or two, may assume the characters of true cholera. The preliminary looseness in such cases is called the "premonitory diarrhœa." Whether this looseness is specifically related to the subsequent attack, or is of an ordinary catarrhal or bilious type and acts simply by predisposing to the specific disease, has not been determined. Possibly, owing to a catarrhal condition—in itself non-specific—the resisting power of the mucous membrane is impaired; possibly, in diarrhœa, the large amount of fluid in the gut affords a favourable medium for the cholera germ to multiply in. Besides diarrhœa, other prodromata, such as languor, depression of spirits, noises in the ears, etc., are sometimes noted.

When true cholera sets in, profuse watery stools, painless or associated with griping, and at first fæcal in character, pour, one after the other, from the patient. Quickly the stools lose their fæcal character, becoming colourless or, rather, like thin rice-water containing small white flocculi in suspension. Enormous quantities—pints—of this material are generally passed by the patient. Presently vomiting, also profuse, at first perhaps of food, but very soon of the same rice-water description, supervenes. Cramps of an agonizing character attack the extremities and abdomen; the implicated muscles stand out like rigid bars, or are thrown into lumps from the violence of the contractions. The patient may rapidly pass into a state of collapse. In consequence principally of the loss of fluid by the diarrhœa and vomiting, the soft parts shrink, the cheeks fall in, the nose becomes pinched and thin, the eyes sunken, and the skin of the fingers shrivelled like a washerwoman's. The surface of the body becomes cold,

Digitized by Google

livid, and bedewed with a clammy sweat; the urine and bile are suppressed; respiration is rapid and shallow; the breath is cold and the voice is sunk to a whisper. The pulse soon becomes thready, weak, and rapid, and then, after coming and going and feebly fluttering, may disappear entirely. The surface temperature sinks several degrees below normal—to 93° or 94° F.; whilst that in the rectum may be several degrees above normal—101° to 105° F. The patient is now restless, tossing about uneasily, throwing his arms from side to side, feebly complaining of intense thirst and of a burning feeling in the chest, and racked with cramps. Although apathetic, the mind generally remains clear. In other instances the patient may wander or may pass into a comatose state.

This, the "algid stage" of cholera, may terminate in one of three ways—in death, in rapid convalescence, or in febrile reaction.

When death from collapse supervenes, it may do so at any time from two to thirty hours from the commencement of the seizure, usually in from ten to twelve. On the other hand, the gradual cessation of vomiting and purging, the reappearance of the pulse at the wrist, and the return of some warmth to the surface may herald convalescence. In such a case, after many hours' absence, the secretion of urine returns, and in a few days the patient may be practically well again. Usually, however, a condition, known as the "stage of reaction," gradually supervenes on the algid stage.

Reaction: cholera typhoid.—When the patient enters on this stage the surface of the body becomes warmer, the pulse returns, the face fills out, restlessness disappears, urine may be secreted, and the motions diminish in number and amount, becoming bilious at the same time. Coincidently with the subsidence of the more urgent symptoms of the algid stage and this general improvement in the appearance of the patient, a febrile condition of greater or less severity may develop. Minor degrees of this reaction generally subside in a few hours; but in more severe cases the febrile state becomes aggravated, and a condition in many respects closely resembling typhoid fever, "cholera typhoid," ensues. This febrile or possibly typhoid state may last from four or five days to perhaps a fortnight or even longer. In severe cases the face is flushed, the tongue brown and dry, and there may be delirium of a low typhoid character with tremor and subsultus; or the patient may sink into a peculiar torpid condition. The motions are now either greenish or like pea-soup, and may contain

Digitized by Google

a larger or smaller amount of blood; at the same time they are very offensive. The reappearance of urine may be delayed from two to six days; at first scanty, high-coloured, cloudy, albuminous and containing casts, it gradually becomes more copious, paler, and with less albumen. Though at first the urine is very deficient in urea, in uric acid, and in salts, later the quantity of these substances may exceed for a time the normal.

During the stage of reaction death may occur from a variety of complications; from pneumonia, from enteritis and diarrhœa, from asthenia, or from such effects of uræmic poisoning as coma and convulsions.

In cholera there is a considerable variety in the character of the symptoms and in their severity, both as regards individual cases and as regards different epidemics. It is generally stated that during an epidemic the earlier cases are the more severe, those occurring towards the end of the epidemic being on the whole milder.

Ambulatory cases occur during all epidemics. Such cases are characterized by diarrhœa and malaise merely; there is never complete suppression of urine, the diarrhœa never loses its bilious character, and it is not accompanied by cramps. The attack gradually subsides without developing a subsequent stage of reaction.

Cholerine.—In another set of cases the diarrhœa may be somewhat more acute, and the stools assume the well-known rice-water appearance; but the looseness soon ceases without leading to suppression of urine, or to algid symptoms, or even to very severe cramps, and without being followed by a stage of reaction. Such cases are sometimes designated "choleraic diarrhœa" or "cholerine."

Cholera sicca.—A very fatal type is that known as "cholera sicca." In these cases, though there is no, or very little, diarrhœa or vomiting, collapse sets in so rapidly that the patient is quickly overpowered as by an overwhelming dose of some poison, and dies in a few hours without purging or any attempt at reaction. At the post-mortem examination the rice-water material so characteristic of cholera, though it may not have been voided during life, is found in abundance in the bowel. Other cases die suddenly from apnœa caused, apparently, either by coagula in the right heart or by spasm of the pulmonary arterioles, the lungs refusing to transmit the thickened blood. In certain cases, after temporary improvement, relapse may occur and is nearly always fatal.

Hyperpyrexia is an occasional though rare occurrence in cholera.

Digitized by Google

In such the axillary temperature may rise to 107° F., the rectal temperature perhaps to 109° F. These cases also are almost invariably fatal.

Sequelæ.—Cholera is apt to be followed by a variety of more or less important sequelæ, such as anæmia, mental and physical debility, insomnia, pyretic conditions, chronic enterocolitis, nephritis, different forms of pulmonary inflammation, parotitis apt to end in abscess, ulceration of the corneæ, bedsores, and gangrene of different parts of the body. Jaundice occurs at times, and is said to be of the gravest import. Pregnant women almost invariably miscarry, the fœtus showing evidences of cholera.

Morbid anatomy and pathology.—Rigor mortis occurs early and persists for a considerable time. Curious movements of the limbs may take place in consequence of post-mortem muscular contractions. On dissection the most characteristic pathological appearances in cholera are those connected with the circulation and with the intestinal tract.

If death occurred during the algid stage, the surface presents the shrunken and livid appearance already described. On opening the body, all the tissues are found to be abnormally dry. The muscles are dark and firm; sometimes one or more of them are discovered to be ruptured—evidently from the violence of the cramps during life. The right side of the heart and systemic veins are full of dark, thick, and imperfectly coagulated blood, which tends to cling to the inner surface of the vessels. Fibrinous clots, extending into the vessels, may be found in the right heart. The lungs are usually anæmic, dry, and shrunken; occasionally they may be congested and œdematous. The pulmonary arteries are distended with blood, the pulmonary veins empty. The liver is generally loaded with blood; the gall-bladder full of bile; the spleen small. Like all the other serous cavities, the peritoneum contains no fluid, its surface being dry and sticky. The outer surface of the bowel has generally a diffuse rosy red, occasionally an injected appearance. On opening the bowel it is found to contain a larger or smaller amount of the characteristic rice-water material, occasionally blood. The mucous membrane of the stomach and intestine is generally pinkish from congestion, or there may be irregularly congested or arborescent patches of injection here and there throughout its extent. In addition, there may be seen smaller or larger points of ecchymosis in or under the mucous membrane. The changes in the alimentary canal are most marked at the lower end of the ileum, where Peyer's patches and the solitary glands may be seen to be congested and swollen. In some instances the bowel is pale throughout; in many the mucous membrane has a sodden, pulpy appearance from exfoliation of epithelium—possibly a post-mortem change; occasionally, especially towards the lower end of the ileum, a croupous exudation is met with. The mesenteric glands are congested. The superficial veins of the kidneys are full; the medullary portion is much congested, the cortical portion less so; the tubules are filled with granular matter; the epithelium is cloudy, granular, or fatty, and, at a later stage, may be shed. The bladder is empty and contracted. Nothing special is to be noted in the nervous system.

If death occurred during the stage of reaction, the tissues are moist; the venous system is less congested; the lungs are probably congested and

Digitized by Google

œdematous, perhaps inflamed. Very probably there are evidences of extensive enteritis.

Greig has shown that the gall-bladder and biliary passages are frequently invaded by the cholera vibrio and that, as in the case of enteric, this viscus may act as a reservoir of infection (Fig. 89). Occasionally, according to the same authority, cholera may be a septicæmia; the vibrios have been demonstrated in the substance of the lung, kidneys, and in the spleen; they may be excreted in the urine (8 times in 55 cases—Greig).

On microscopical examination of the contents of the bowel during the acute stage of the disease the comma bacillus, in most cases, may be demonstrated. Usually it is in great abundance; occasionally it occurs in almost

Fig. 89.—Cholera bacillus in gall-bladder. (*After Greig, "Ind. Journ. Med. Res."*)

a pure culture in the upper part of the small intestine and duodenum, but it may be very rare in the large gut. Sections of the intestine show the bacillus lying on and between the epithelial cells of the villi and glands.

Diagnosis.—During the height of an epidemic the diagnosis of cholera is generally an easy matter; the profuse rice-water discharges, the collapse, the cold clammy skin, the cyanosis, the shrunken features, shrivelled fingers and toes, the feeble, husky, hollow voice, the cold breath, the cramps, and the suppression of urine, together with the high rate of mortality, are generally sufficiently distinctive. But in the first cases of some outbreaks of diarrhœa, which may or may not turn out to be cholera, and the true nature of which, for obvious reasons, it is of importance

Digitized by Google

to determine, correct diagnosis, though urgently required, may not be so easily attained.

Symptoms resembling true cholera may supervene in the course of an ordinary severe *diarrhœa*, and are very usual in cholera nostras, in mushroom poisoning, in ptomaine poisoning, in the early stages of trichinosis, and in a certain type of pernicious malarial fever. In none of these, however, is the mortality so high as in cholera. It may be laid down, therefore, that epidemic diarrhœa attended by a case-mortality of over 50 per cent. is cholera.

In other forms of diarrhœa it is rare for the stools to be persistently so absolutely devoid of biliary colouring matter as they are in cholera. A careful inspection of the stools sometimes yields valuable information in other ways. Thus, in mushroom poisoning fragments of the mushrooms which caused the catharsis may be seen; in trichinosis the microscope may detect the adult trichina. In choleraic malarial attacks the presence of the malaria parasite in the blood, the periodicity of the symptoms, their amenability to quinine, together with the character of the prevailing epidemic, generally combine to guide to a correct diagnosis.

The detection of the comma bacillus in the stools is now regarded as a positive indication of cholera. It would be rash, however, to affirm that a negative result from bacteriological examination of a single case is conclusive against its being cholera. Moreover, such examinations to be trustworthy have to be made by a skilled bacteriologist.

In the first place the stools should be examined microscopically. If vibrios are present in large numbers they may be detected by their scintillating rotatory movements in hanging-drop preparations, or by their characteristic shape in fæcal films stained by carbol-fuchsin. According to Koch, a rough diagnosis may be made in 50 per cent. of cases by this method. If vibrios are very numerous, plates may be spread direct by means of a platinum loop on alkaline agar, or Dieudonné's medium (Appendix, p. 894). When they are in small numbers—(*a*) Alkaline peptone water should be inoculated with the loopfuls of the fluid stool and incubated for seven hours. (*b*) Any pellicle present on the surface of the broth should be examined in stained films or by means of the hanging-drop method. (*c*) If vibrios are scanty, reinforce by inoculating a second alkaline peptone tube and incubating for a further six to eight hours, and plate out on alkaline agar. (*d*) An emulsion of colonies from the plate or from an agar slope subculture should be agglutinated against the specific antiserum in high titre.

Digitized by Google

An agglutination of over 1 : 1,000 with a specially prepared serum is strongly suggestive of the true cholera vibrio, which may then be subjected to special biochemical tests.

The carrying out of the full technique of identification demands a considerable amount of time, and as promptness is the first essential in cholera diagnosis, be it of acute cases or of "carriers," other methods of rapid and more or less accurate diagnosis have been devised. Such a one is Bandi's method, which consists of inoculating the suspected fæces into peptone water containing agglutinating serum of such strength as to clump the *V. choleræ* in high dilution. Within as short a period as three hours' incubation, it is said that agglutination visible to the naked eye will be present. This method, when employed in a large number of cases, necessarily consumes a large quantity of immune serum.

A modification has been employed by Davies and the Editor in the rapid diagnosis of cholera cases and carriers, with satisfactory results. The advantages of such a rapid method are obvious: positive reports may be obtained on a large number of cases in as short a period as eighteen hours, and as many as 200 stools may be examined by one worker during the course of a morning's work. The following are the stages in the technique :—

1. Inoculate a platinum loopful of fæces into peptone water, 1 per cent. peptone, 1 per cent. NaCl, made distinctly alkaline to litmus.

2. Incubate for eighteen hours.

3. Place a drop of the resulting growth on the slab of Garrow's agglutinometer (Appendix, p. 899), together with a drop of 1 : 80 anticholera serum. The resulting mixture will give a dilution of cholera serum 1 : 160. On the next partition drop an equal quantity of normal saline, together with a drop of the peptone culture, to act as a control. Rotate for three minutes. If vibrios are present a definite agglutination will be obtained. This can be confirmed later by agglutinating with cholera serum in still higher dilutions. It is recommended that stock bottles (with rubber caps) of cholera serum preserved with 0·5 per cent. carbolic acid, in dilutions 1 : 80, 1 : 160, 1 : 320, 1 : 640, be kept. If an agglutination is obtained with the lower dilutions it may subsequently be titrated with the higher ones. It is necessary to cleanse the slab thoroughly with alcohol and ether, using a clean handkerchief, and to warm it slightly over a flame before use, or else the resulting emulsion of the culture and serum will not mingle properly on the slab.

4. The peptone culture can then be spread with a platinum loop on Crendiropoulo's agar (alkaline agar), and a pure culture obtained by this means. The cholera colonies can be easily recognized by their transparent bluish-grey appearance. The hæmolytic and sugar tests may then be applied. It has been found that vibrios agglutinating with specific serum in high dilutions invariably give correct sugar, hæmolytic, and cholera-red reactions.

In an autopsy on a suspected case of cholera at least two sections of the small gut, each about 5 in. in length—one just

Digitized by Google

above the ileo-cæcal valve, the other in the middle of the ileum—should be ligatured, cut off, dropped into sterile saline, and sent to a bacteriological laboratory as soon as possible for examination.

An agglutination reaction is not obtainable from the blood-serum during the acute stage, but it is present after eight to ten days from the commencement of the disease, reaching its maximum in four weeks; it may attain a titre of 1 : 1,000.

Caution.—Greig has found that some normal serums agglutinate the cholera vibrios microscopically in a dilution of 1 : 90, and that fatal cases rarely give a higher agglutination than 1 : 40.

Mortality.—The average case-mortality in cholera amounts to about 50 per cent. Some epidemics are more deadly than others. As already mentioned, the mortality is greater at the earlier than at the later stages of an epidemic. To the old, the very young, the pregnant, the subjects of grave organic disease—particularly of the liver, kidneys, and heart—the dissipated, the underfed, and the feeble, the danger is very great.

Quarantine prevention.—Theoretically, quarantine should be an efficient protection against the introduction of cholera into a community; practically, it has proved a failure. Unless they are stringent and thoroughly carried out, quarantine regulations can be of little use. Even if the utmost care, intelligence, and honesty succeed in excluding individuals actually suffering from cholera, or likely within a reasonable time to suffer from cholera, there is yet no guarantee that the germ of the disease may not be introduced. Koch, Greig, and others have shown that sometimes the dejecta even of individuals who have been associated with the disease and are apparently in good health, and who have not suffered or may not subsequently suffer from choleraic disease, may yet contain, and for some time continue to contain, the cholera vibrio. In 271 fatal cases Greig found the vibrio in the gall-bladder, a situation favouring persistence in the event of recovery. He also found that convalescent patients passed vibrios in their stools for as long as forty-four days. During the epidemic of 1911, in Naples, 10 per cent. of healthy contacts had cholera vibrios in their stools and continued to pass them for twelve days. The healthy carrier, as in the case of enteric and other intestinal infections, has now to be reckoned with as the starting-point of an epidemic. It was estimated that, in the Naples epidemic already cited, 90 per cent. of the cases were due to direct contact with patients or healthy carriers. For the recognition of the carrier state it is necessary, following the technique given above, to

Digitized by Google

examine the stools of all contacts for the vibrio. A small dose of calomel to clear out the contents of the small intestine greatly increases the chance of recovering the vibrio from stools. This is the only scientific method of conducting a reliable quarantine.

So far from ordinary quarantine proving a defence against cholera, it may actually increase the risk of an epidemic. This it does by fostering a false sense of security, and so leading to neglect of those well-proved guarantors of the public health—domestic, municipal, and personal cleanliness, and a pure water and food supply; and further, in consequence of the intimate association of a number of individuals in a quarantine station, the number of carriers is likely to be increased. The Bordet-Gengou reaction, using an emulsion of the vibrio as an antigen, has been advocated as a method of detecting carriers by serum diagnosis, but it is too complicated to be practicable.

The system to which Great Britain apparently owed her immunity during recent epidemics on the continent of Europe is a practicable and, in civilized conditions, an efficient one. Under this system only ships which were carrying or which had recently carried cholera patients were detained; and even these merely till they could be thoroughly disinfected. Thus inconvenience and loss to travellers and merchants were small, and the temptation to conceal cases of the disease or to evade regulations was proportionately minimized. Any cholera cases were isolated in suitable hospitals, the rest of the crew and passengers, although supervised for a time, being given free pratique. At the same time attention was not diverted from the sanitation of towns, especially of seaports—the measure mainly relied on. Suspicious cases occurring on shore were at once reported to the sanitary authorities and promptly dealt with, fomites being destroyed or disinfected at as little cost and inconvenience to individuals as possible. Every endeavour was made to prevent fæcal contamination of the public water supply.

Of late years in India preventive measures are being conducted much on the same lines, attention being given to sanitation rather than to quarantine. During the great religious festivals the sanitary condition of the devotees is looked after as far as practicable, special care being given to provide them with good drinking- and bathing-water. Many of the large Indian towns now enjoy an abundant and pure water supply; and civilized systems of night-soil conservancy and other important sanitary measures are being gradually introduced, and, in the case of more than one great city, with the most gratifying results.

Digitized by Google

Among the troops in India, on the appearance of cholera in their neighbourhood, special protective measures are promptly instituted, elaborate directions having been drawn up for the guidance of medical officers.

Incubation period.—All quarantine and protective systems must take cognizance of the fact that, although cholera may declare itself within a few hours of exposure to infection, it may also do so at any time up to ten days thereafter; three to six days may be set down as the usual duration of the incubation period.

Anticholeraic inoculations.—Inoculation against cholera was first introduced by Ferran in Spain in 1883; owing to defects in the preparation of the cultures, the results were not encouraging. In 1893 Haffkine, after elaborate experiments on the lower animals, commenced a system of anticholera vaccinations; the first culture he used proved to be too virulent, but subsequently a milder vaccine was prepared by cultivating the strong vaccine in artificial media at a temperature of 39° C., and in an atmosphere of oxygen kept constantly renewed. Having satisfied himself that the subcutaneous injection of a mild followed by a more virulent vaccine conferred immunity against the cholera vibrio in the lower animals, Haffkine, with the approval and aid of the Government, proceeded to use such vaccines in man on a large scale. Up to 1895, 70,000 injections of living cholera bacilli had been made in 43,179 Indians. In no instance did any bad result ensue. During the recent war many millions of anticholeraic inoculations were made. The initial dose is ½ c.c. of an emulsion of 4,000 millions, followed seven to ten days later by a second inoculation of 1 c.c. containing 8,000 millions. Experience has shown that even larger doses can be easily tolerated. The local reaction is, generally speaking, a very mild one. There may be œdema and a painful infiltration at the site of the injection, rarely followed by systemic disturbance. The vaccine is put up by the Royal Army Medical College, in bottles fitted with a rubber cap.

Several strains of cholera vibrios are used. They are inoculated into Roux bottles containing "pea-extract agar" and grown for forty-eight hours. The growth is washed off with normal saline, and the emulsion counted, dark-ground illumination being employed. The emulsion is then heated to 55° C. for one hour, after which 1 per cent. carbolic is added. The emulsion thus sterilized is finally diluted down so as to contain 8,000 million vibrios per c.c. of saline and 0·5 per cent. carbolic. *Dose:* Two subcutaneous injections at an interval of 7–10 days, the first of ½ c.c. and the second of 1 c.c.

The immunity thus produced does not seem to be a very persistent one, lasting at the maximum for three or four months.

Digitized by Google

Powell's results in Assam are highly favourable—namely, 198 cases of cholera with 124 deaths among 6,549 non-inoculated tea-garden coolies, against 27 cases and 14 deaths among 5,778 inoculated coolies. Had the incidence of cholera been the same in both classes, the inoculated would have had 174 instead of 27 cases, and 109 instead of 14 deaths. In 1912, 8,000 Europeans were inoculated in Batavia, and among these there was only one death from cholera as against 15 deaths amongst 2,700 uninoculated.

Subsequent experience, particularly that obtained during the Balkan War of 1913, in Batavia in 1915 and 1916, and in the Great War, has gone far to confirm these earlier impressions of the value of Haffkine's vaccinations. The cholera vaccine may be mixed with typhoid, paratyphoid-A and -B, though it is doubtful whether this course is advisable.

Personal prophylaxis.—During cholera epidemics great care should be exercised to preserve the general health; at the same time, anything like panic or apprehension must be sedulously discouraged. Fatigue, chill, and excess—particularly dietetic or alcoholic excess—are to be carefully avoided. Visits to cholera districts should be postponed if possible, seeing that the new-comer is especially liable to contract the disease. Unripe fruit, over-ripe fruit, shell-fish, food in a state of decomposition, and everything tending to upset the digestive organs and to cause intestinal catarrh, are dangerous. Melons, cucumbers, and the like deserve the evil reputation they have acquired. Purgatives —particularly saline purgatives—unless very specially indicated, should never be taken at these times. All drinking-water, and all water in which dishes and everything used in the preparation and serving of food are washed, should be boiled. Mere chlorination of the water with bleaching powder ($CaClO,Cl$) giving 1·3 parts of chlorine per million, or added to water in the proportion of 2 grm. of the powder to every 110 gallons, is not entirely reliable. Sodium bisulphate tabloids (2 grm. to $1\frac{3}{4}$ pints of water), by liberating sulphuric acid, provides a most useful method of sterilizing water for personal use, as for instance in a water-bottle. Filters —except perhaps the Pasteur-Chamberland filter—are not for the most part to be relied on; in many instances they are more likely to contaminate the water passed through them than to purify it. A good plan in a household or in public institutions is to provide for drinking purposes an abundant supply of weak tea or lemon decoction, the supply being renewed daily; such a plan ensures that the water used in the preparation of the drink has been boiled. All food should be protected from flies.

Digitized by Google

Diarrhœa occurring during cholera epidemics should be promptly and vigorously treated.

Treatment.—During cholera epidemics it is customary to establish depots where sedative and astringent remedies for the treatment of diarrhœa are dispensed gratuitously. Experience seems to encourage the belief that by such means incipient cholera may be aborted during the stage of premonitory diarrhœa. Of the various drugs used with this view, chlorodyne, or chlorodyne with brandy, is the most popular. Lead and opium pill; chalk, catechu, and opium mixture; compound kino powder; aromatic powder of chalk and opium; a pill of opium, asafœtida, and black pepper; dilute sulphuric acid and laudanum—are among the drugs more commonly employed for this purpose. Whether true cholera can be cut short in this way or not, it is certainly in the highest degree advisable at such a time to neglect no case of diarrhœa, but to insist on rest, warmth, and the greatest prudence in feeding in all cases of intestinal catarrh or irritation.

Until recently, the only treatment of proved value in cholera was the purely symptomatic and expectant one. If our efforts have failed to counteract the premonitory diarrhœa, attention should be given to maintaining the patient in as favourable a condition as possible to struggle against the poison of the disease. He should be kept strictly in the horizontal position, in a warm bed, and in a well-ventilated but not too cold room. His thirst should be treated by sips of iced water or of soda-water, or champagne, or brandy and water. Copious draughts, as they are likely to provoke vomiting, are usually condemned. It does not follow from this that they are harmful; the emesis contributes to the elimination of germ and toxin. Cramps may be relieved by gentle frictions with the hand or with ginger-root, by a small hypodermic injection of morphia, or, these failing, by short chloroform inhalations. The surface of the body should be kept dry by wiping it with warm dry cloths, and the surface heat maintained by hot-water bottles or warmed bricks placed about the feet, legs, and flanks. The patient must not be allowed to get up to pass his stools; a warmed bed-pan should be provided for this purpose. All food should be withheld while the disease is active.

The only drug which has received anything like approbation is that known as "bolus alba." It consists of kaolin 200 grm. (7 oz.) in 400 c.c. (14 oz.) of water. This is the dose, but if there is vomiting the dose may be repeated, and sipped in small amounts at a time.

Rogers's treatment.—Rogers has introduced a method of treating cholera by intravenous injection of hypertonic saline solution,

Digitized by Google

which promises well. He claims that since the introduction of his method the case-mortality from this disease in the Calcutta Medical College Hospital has been greatly reduced; and others who have practised his method have in most instances had equally good results. Owing to collapse of the veins it is generally necessary to cut down on to them in order to insert the cannula. The principle of the treatment is based on the fact that not only is the water-content of the blood reduced one- to two-thirds, according to the severity of the case, but in addition there is a loss of the saline constituents. Hence the necessity for supplying the latter. The hypertonic solution * is composed as follows: Sodium chloride, 120 gr.; potassium chloride, 6 gr.; calcium chloride, 4 gr.; sterilized water, 1 pint. The fluid in the containing bottle should be at a temperature of about 100° F. if the rectal temperature is below 99° F.; if the latter is above 100° F., as there is risk from hyperpyrexia, the injection should be given at a temperature between 80° and 90° F. This solution Rogers introduces by means of a special stopcock cannula and transfusion bulb at the rate of not more than 4 oz. a minute, the flow being slowed down to 1 oz. if distress or headache supervene. From three to six pints should be given if possible. As the injections may have to be repeated several times, the cannula, suitably secured and protected, should be left in the vein till symptoms indicate that the acute stage is subsiding. At the same time Rogers gives permanganate of potassium in solution or in pill by mouth up to 50 gr. a day as a means of destroying the toxins formed in the alimentary canal—2 gr. every quarter of an hour for two hours, then every half-hour till the stools are coloured green. These pills are made up with vaseline and coated with salol.

With the intravenous saline Rogers combines hypodermic injections of atropine, $\frac{1}{100}$ gr., morning and evening; his statistics would indicate, and attribute to the atropine, a further reduction of mortality to one-half. The principles upon which Rogers's treatment is founded may be stated as follows:—

1. A blood-pressure below 70 mm. of mercury indicates a dangerous collapse, and a specific gravity of the blood of 1063 or over. In the acute stage of the disease the specific gravity of the blood varies between 1060 and 1072, the normal figure for a European adult being 1058 and for an Eastern native 1056.

* Bayliss points out that the vessel walls are permeable to salts, which thus pass out into the tissues, so that the additional fluid is not retained in the circulatory system; he therefore suggests that a colloid, such as gum acacia, which has been employed so successfully in shock from hæmorrhage, would be an improvement. The gum acacia should be given in a 6- or 7-per-cent. solution in 0·9-per-cent. sodium-chloride solution.

Digitized by Google

2. A specific gravity of 1063 indicates a loss of half the fluid from the blood and for correction an injection of 3–6 pints.

3. The subsequent fall of blood-pressure to 70 mm. or under, or rise in the specific gravity to 1063, indicates repeated injections morning and evening.

The specific gravity of the blood is estimated by employing a series of small bottles of aqueous glycerin with specific gravities increasing by 2° per bottle from 1048 to 1070. The specific gravity may be controlled by employing a urinometer. Blood from the patient is dropped on to the surface of the fluid in the bottles by means of a capillary pipette. A drop of blood which remains stationary in the centre of the glycerin solution of a given strength indicates its specific gravity.

Rogers considers that the occurrence of *uræmia* in cholera is the result of the development of an acidosis. In such cases he recommends the injection, subcutaneously or per rectum, of a 2- to 3-per-cent. solution of sodium bicarbonate, together with hypertonic saline, if the specific gravity of the blood is low; if the specific gravity of the blood is high or normal, it should be given intravenously at first, and subsequently by rectum. By employing the methods advocated, Rogers now claims that in a series of 638 cases from 1915–17 his mortality rate is 19·1 per cent., the fall being mainly due to decrease in the deaths from uræmia. He gives the following statistics to demonstrate the effects of various forms of treatment of cholera in Calcutta :—

Years	No. of Cases	Deaths	Mortality per cent.	Recoveries per cent.
	(*a*) *Normal saline subcutaneously and per rectum*			
1895–1905	1,243	788	59·0	41
	(*b*) *Normal saline intravenously*			
1906	112	57	51·9	49·1
	(*c*) *Normal saline subcutaneously and per rectum*			
1907	158	94	59·5	40·5
	(*d*) *Hypertonic saline intravenously*			
1908–9	294	96	32·6	67·4
	(*e*) *Hypertonic saline plus permanganate*			
1909–14	858	222	25·9	74·1
	(*f*) *Hypertonic saline, permanganate, and alkalis*			
1915–17	638	122	19·1	80·9

Other practitioners advocate the use of adrenalin solution injected hypodermically—10 min. of a 1 : 10,000 solution every three hours.

Recent experience has shown that strong solutions of hypertonic glucose (25 per cent.) given intravenously may act beneficially in suppression of urine.

Dr. Cox of Shanghai has had encouraging results from continuous, prolonged, slow intravenous injections of isotonic saline fluid given by a special apparatus placed 2½ ft. above the level of the patient's arm. The flow is kept up for several hours, at a rate of 2 oz. per minute, as long as there is danger from collapse.

Digitized by Google

The intravenous injection of Salimbeni's anticholera serum in doses of 40 to 100 c.c. has been favourably reported upon by some observers.

During the stage of reaction, should purging persist, large doses of salicylate of bismuth with a little opium may prove of service. In these circumstances massive rectal injections of tannin 1 oz., gum arabic 1 oz., warm water 1 quart, are of use. If the secretion of urine is not quickly restored, large hot poultices over the loins, dry-cupping of the same region, and the judicious use of bland diluents should be had recourse to. Stimulating diuretics are dangerous. Injections of digitalin, gr. $\frac{1}{100}$, may be given to stimulate the cardiac action. Retention of urine must be inquired about, and the region of the bladder frequently examined, and, if necessary, the catheter employed. In the event of constipation, purgatives must be eschewed and simple enemata alone used.

In cholera convalescents the diet for a time must be of the simplest and most digestible nature—diluted milk, barley-water or rice-water, thin broths, meat juice, and so forth—the return to ordinary food being effected with the greatest circumspection.

Cholera typhoid must be treated much as ordinary enteric fever.

Precautions.—It must never be forgotten by those responsible for the management of cholera cases that through their discharges such patients are a danger to the community, and that those discharges may contain the vibrio in some instances up to fifty days after the attack. Further, that though the germ dies in a few hours if dried, it preserves its vitality for many days if kept moist, as, for example, in damp, soiled linen; that it may live for months as a saprophyte in water or damp soil; and that it is not killed by ordinary cold. Therefore, all discharges and soiled linen from cholera cases should be immediately disinfected in a 2½-per-cent. cresol solution, or destroyed, and every precaution must be taken during convalescence, as well as during the acute stage, to prevent contamination of wells, public water supply, drinking and table vessels, and food. The domestic fly and other vermin as vectors of the germ must not be overlooked. When the ground has been fouled by dejecta or vomit it should be disinfected with cresol, or raked over with hot ashes and soaked with benzene and set alight. Wells and water supplies during a cholera epidemic should be treated with potassium permanganate till the water becomes pink; an appropriate strength is of 60 gr. to the gallon of water, or 1 oz. to 2,000 gallons. The water should be left till colourless for twenty-four hours, and all vegetation and aquatic fauna removed.

Digitized by Google

CHAPTER XXIX

THE DYSENTERIES

UNTIL comparatively recently, and not until the rôles of *Bacillus dysenteriæ*, *Entamœba histolytica*, and certain other protozoal and metazoal parasites had been definitely ascertained, the classification of the group of diseases covered by the term dysentery—that is to say, clinical conditions associated with the occurrence of blood and mucus in the stools, together with griping and tenesmus—could be made only on a clinical and empirical basis. The discoveries referred to have made possible a much more satisfactory classification which, from the point of view of prevention and cure, has proved of the greatest practical value.

Three types of dysentery, correlated to three different classes of parasites, are now definitely established. They, though quite distinct, are not mutually exclusive, for one type may be superimposed upon and complicate another; moreover, any or all of them may complicate some general disease, such as malaria or enteric. Henceforth, therefore, the term "dysentery" must be regarded as indicating a group of symptoms merely, and not a particular and etiologically distinct disease.

The principal forms of dysentery and their respective parasites are as follows:—

I. BACTERIAL—

BACILLARY DYSENTERY:
Bacillus dysenteriæ Shiga, or Flexner-Y.

II. PROTOZOAL—

AMŒBIASIS—Amœbic dysentery, Liver abscess, etc.:
Entamœba histolytica.

BALANTIDIUM DYSENTERY:
Balantidium coli.

III. VERMINOUS—

BILHARZIAL DYSENTERY:
Schistosoma mansoni, S. japonicum, or S. hæmatobium.
Œsophagostomum apiostomum.

Digitized by Google

The present chapter is devoted to bacillary dysentery. In Chap. XXX. amœbiasis will be described, together with hepatic abscess, which is now known to be a feature of that infection. It is appropriate to include a similar protozoal infection, caused by *Balantidium coli*, in the same chapter, which also includes bilharzial dysentery.

The differential diagnosis of the dysenteries, an extensive subject, is dealt with separately at the end of Chap. XXX.

I.—BACILLARY OR EPIDEMIC DYSENTERY

Definition. — An acute epidemic disease due to invasion of the mucosa of the large intestine by specific bacteria (*B. dysenteriæ* Shiga and Flexner-Y), accompanied by pyrexia, symptoms of toxic absorption, and the discharge of blood-stained mucus in the stool. In severe cases colliquative necrosis of the mucosa may take place and quickly lead to death. In the milder forms the clinical symptoms may be those of a simple diarrhœa.

Geographical distribution.—Epidemics of bacillary dysentery have occurred at various times, both in the tropics and in temperate countries, though at the present day they are of greater intensity and frequency in those countries in which the insanitary habits of the natives and more primitive conditions of life lend themselves to the spread of the disease. In Europe, bacillary dysentery is to-day mainly an institutional disease, occurring not infrequently as outbreaks in lunatic asylums, prison camps, and military barracks. It is a disease which has dogged the footsteps of armies in every big campaign. Apparently it was the scourge of Napoleon's armies in the retreat from Moscow, and it was a source of considerable disability and death in the South African War of 1900–2. In France and the Near East, epidemics of formidable magnitude were recorded during the recent War. The casualties caused by this disease amongst the forces in Gallipoli, Salonika, Egypt, Palestine, Mesopotamia, and East Africa were numerous. As a cause of invaliding and death, bacillary dysentery was in these campaigns as important as was enteric in former wars. Epidemics have been reported from the Arctic Circle, even among the Eskimos, while it is common in the labour camps and coolie lines on the tea and rubber plantations of the East and the coconut groves of the Pacific islands. From time to time epidemics of considerable virulence have struck down the whole personnel of ships carrying coolies to Queensland and the Pacific islands.

Epidemiology. — In the tropics and subtropics bacillary

Digitized by Google

dysentery appears to observe a definite seasonal incidence. It is certainly most prevalent during the rainy season and for a short period subsequent to this, but in those regions which have a definite seasonal climatic variation it is most prevalent in the autumn months, as for instance September and October, while minor epidemics may occur in the early spring months as well. During the hot dry African summer the disease appears to be in abeyance.

Its spread from man to man takes place either by direct or by indirect contagion.

Direct contagion by means of fæces can only occur, as a rule, among primitive communities in which the ordinary sanitary laws are either unknown or disregarded. Its occurrence in lunatic asylums is attributed to the personal habits of the inmates, which lend themselves to the spread of infection, or even, under more normal conditions, to the incautious use of instruments such as enema syringes.

Indirect contagion. (*a*) *Flies.*—There appears to be little doubt that houseflies (*Musca domestica*) act as carriers of the infection. The seasonal incidence of bacillary dysentery corresponds in a remarkable manner with the maximum prevalence of these pests. This is a noteworthy fact in European countries, as well as in the tropics; though in hot countries, when climatic conditions are inimical to the propagation of the housefly, bacillary dysentery is not in evidence.

In 1910 the Editor demonstrated dysentery bacilli, in considerable numbers, in the intestinal tract of houseflies taken in an endemic area; this finding was subsequently confirmed. Under experimental conditions, dysentery bacilli can survive in the intestinal canal of flies for at least five days, as has been found to be the case with typhoid bacilli also (Graham-Smith).

The housefly is able to propagate dysenteric infection in two ways—firstly, by its habit of regurgitation preparatory to feeding; and secondly, by means of its fæces. The latter is probably the more common method.

Buxton has found that the intestinal canal of the majority of houseflies caught in Mesopotamia contained human fæces. One can therefore understand the importance of this insect in the spread of the disease.

(*b*) *Water* may possibly act as a medium of infection. It has been shown that the bacillus can survive in drinking-water for over three weeks, but not for so long a period if exposed to the sun or when associated with numbers of other putrefactive micro-organisms. When all water is chlorinated (bleaching powder

Digitized by Google

1 : 1,000,000) or boiled, it is difficult to see what part it can play in the spread of extensive epidemics. For the same reason, food, if properly cooked, and preserved from contamination, need not be regarded as a source of danger.

(*c*) *Dust.*—It has been shown that the dysentery bacillus can withstand a certain amount of desiccation, and it has been suggested that powdered fæces when mingled with dust may aid the spread of epidemics; but in the tropics, especially in arid desert regions where everything is sterilized by the powerful rays of the sun, there is no reason to suppose that fine dust or sand acts as a source of infection, except, it may be, indirectly by irritating the intestinal mucosa and so rendering it more susceptible to the action of the dysentery bacillus conveyed in some other medium.

Etiology.—Celli and Fiocca, in their researches into the etiology of dysentery, believed that it was caused by a variety of *B. coli communis* which, under certain conditions, acquired pathogenic properties. These ideas were dispelled by the discovery of *B. dysenteriæ* by Shiga in 1897, and confirmed in the same year by Kruse in Germany. The organism has therefore been known by some as the *Shiga-Kruse bacillus.*

Shiga's bacillus is a rod-shaped Gram-negative organism 1 to 3 μ in length by 0·4 μ in breadth; it is non-motile, but exhibits very active Brownian movement. Vedder and Duval have demonstrated numerous lateral flagella of great fineness; no spore formation occurs. On agar and gelatin it grows as a thin smooth film with regular margins, and on agar and MacConkey plates its colonies much resemble those of the typhoid bacillus; they are regularly round, light-blue in colour, and dew-like. It produces no liquefaction of gelatin, and grows as a transparent, almost invisible, layer on potato. After a brief preliminary acid production in milk, it gives rise to a gradually increasing alkalinity. With solutions of the various sugars (*see* Table on p. 408) it produces acidity in glucose, but is inert in this respect in the rest of the series; it does not produce indol in peptone water. It is agglutinated in high dilutions by the serums of patients suffering from the disease. It occurs in considerable numbers in dysenteric lesions, and in the mucous stools of the corresponding period.

Varieties of Shiga's bacillus resembling that organism in its sugar reactions, *but forming indol* and not agglutinating with Shiga-immune serum, have been credited with the causation of dysentery. Several species, the bacillus of Schmitz, d'Herelle, the *B. ambiguus* of Andrewes, the para-Shiga + or − of Dudgeon, have been described in the last few years. Their etiological importance is at present doubtful.

Cultures of Shiga's bacillus are extremely toxic to laboratory animals, especially the rabbit; and in these animals it produces only exceptionally lesions characteristic of dysentery, though the filtered toxins when injected intravenously produce necrosis of

Digitized by Google

the large intestine, on which they appear to exert some selective action. In two experiments in man, one intentional, the other accidental, ingestion of pure cultures was followed, within a short time, by well-marked symptoms of dysentery. Considerable work has been done in immunizing both the larger and smaller laboratory animals against this bacillus; the serum thereby obtained has been proved to exert considerable protective as well as curative properties.

The causal relationship between this bacillus and the disease is practically conclusive.

TABLE SHOWING THE MORPHOLOGICAL AND CULTURAL CHARACTERS OF BACILLUS DYSENTERIÆ AND THE ALLIED GROUP OF MICRO-ORGANISMS AFTER TWENTY-FOUR HOURS' INCUBATION AT 37° C.

ORGANISM	MOTILITY	GLUCOSE	LACTOSE	DULCITE	SACCHAROSE	MANNITE	MALTOSE	INDOL	GELATIN	LITMUS MILK
B. typhosus	+	A	—	—	—	A	A	—	—	A
B. paratyphosus-A	+	AG	—	AG slowly	—	AG	AG	—	—	A
B. paratyphosus-B	+	AG	—	AG	—	AG	AG	—	—	A later Alk.
B. dysenteriæ (Shiga)	—	A	—	—	—	—	—	—	—	A later Alk.
B. dysenteriæ (Flexner-Y)	—	A	—	—	—	A	A or —	+ or —	—	A later Alk.
B. enteritidis (Gaertner)	+	AG	—	AG	—	AG	AG	—	—	A later Alk.
B. fæcalis alkaligenes	+	—	—	—	—	—	—	—	—	Alk.
B. coli communis	+	AG	AG	AG	—	AG	AG	+	—	A.C.
B. acidi lactici (Hüppe)	—	AG	AG	—	—	AG	AG	+	—	A.C.

\+ In motility column = presence of motility; in gelatin = liquefaction; in indol = presence of indol.
± = variable; sometimes positive, sometimes negative.
— In motility column = absence of motility; in gelatin = no liquefaction; in indol = absence of indol; in other columns = no change.
A = acid production; AG = acid and gas production; C = clot in milk. Alk. = development of alkalinity.

Flexner's bacillus (the Flexner-Y group).—In 1900 an organism morphologically similar to Shiga's bacillus, but differing in the production of acid from mannite as well as glucose, producing indol from peptone somewhat irregularly, and inagglutinable with Shiga-immune serums, was isolated from cases of dysentery in Manila by Flexner. Since that date a very large number of organisms belonging to this group have been described. Among the number may be cited the bacillus of Strong and the Y bacillus of Hiss and Russel, both of which at first were thought to differ in their biochemical and serological reactions, but this is now known not to be the case. There

Digitized by Google

(*P. Manson-Bahr, del.*)

Fig. 1. Fig. 2.

Fig. 1.—AMŒBIC DYSENTERY : Typical patches of infiltration and ulceration of ascending colon.

Fig. 2.—BACILLARY DYSENTERY (Shiga infection) : Colliquative necrosis of lower portion of ileum, showing characteristic green coloration of the destroyed mucous membrane.

INTESTINAL LESIONS IN AMŒBIC AND BACILLARY DYSENTERY. Half nat. size.

PLATE XVII

Digitized by Google

Digitized by Google

has been so much confusion as regards this group that one welcomes any solution of the problem. From the recent work of Andrewes and Inman on a very large number of strains of the Flexner-Y—*a mannite-fermenting group*—one can state definitely that the organism does not adhere to one constant type, as does Shiga's bacillus, but differs greatly in the toxicity of the various strains and in their antigenic properties. The only basis for satisfactory sub-grouping is a serological one, and that has now been done by Murray, Andrewes, and Inman. From their work it appears that five definite strains of the bacillus can be recognized, termed respectively V, W, X, Y, Z, and for their recognition five specially prepared homologous serums are necessary. A pooled serum of these five components is now provided for laboratory purposes and may be employed for the recognition of the bacillus.

The so-called atypical, pseudo, paradysentery bacilli, or inagglutinable forms, apparently play no part whatever in the etiology of bacillary dysentery. There is no valid reason for incriminating these any more than for incriminating organisms which obviously ferment lactose. They may be separated from the true dysentery bacilli by means of the following test:—

Michaelis's acid agglutination test.—Michaelis has found that a series of dilutions of acetic acid with caustic soda which compose a series of ascending hydrogen-ion concentrations may agglutinate certain bacilli. Fresh agar emulsions of bacteria in distilled water, added to the acid solutions and incubated for two hours at 37° C., may or may not show agglutination. Many other organisms, including *B. typhosus*, *B. paratyphosus*, *B. coli*, and nearly all the so-called inagglutinable or paradysentery organisms, are agglutinated in this manner, but the true dysentery bacilli, Shiga and Flexner-Y, are not.

In the opinion of the Editor, atypical bacilli held to be responsible for bacillary dysentery may be due to deterioration of the fæcal specimens. When working with absolutely fresh blood and mucus passed in the acute stages of the disease, his observations, based upon extensive practical experience, show that the isolation of typical Shiga and Flexner-Y organisms presents no great difficulty.

General observations.—It is apparently the case that the Shiga and Flexner bacilli are encountered in sporadic cases and in some epidemics without a preponderance of any one particular type; but it may be said that Shiga's bacillus is of more frequent occurrence in the tropics than in temperate zones, and that it is responsible for the most severe clinical forms of the disease, and consequently for the most virulent epidemics. Pathologically it is concerned with the production of necrosis of the gut, of arthritis, and other complications. Fatal Flexner-Y cases are seldom observed; in other words, there can be no question that Shiga's bacillus is by far the more important of the two.

Pathology.—The earliest lesions of bacillary dysentery are confined to the solitary follicles of the large intestine, and result in a sinuous "snail-track" ulceration of the free folds of mucous membrane. In very acute

Digitized by Google

cases the process consists of intense hyperæmia of the large intestine, which eventually culminates in gangrene of the mucosa of the whole of the colon, as well as of the last 2–3 ft. of the ileum. Exceptionally the whole of the mucosa of the small intestine may be involved.

As a general rule, the lesions characteristic of bacillary dysentery are most pronounced in the lower part of the intestinal canal, from the sigmoid flexure to the anal canal. In the stage of necrosis the large gut is contracted so as to resemble an elastic tube, and the mucous membrane is converted into a rigid, resistant, olive-green or blackish substance. (Plate XVII., Fig. 2.) Its colour is thought to be due to the staining of the necrotic tissue by bile pigments. Occasionally this necrosis may have a patchy distribution affecting especially the descending and pelvic colons. There are many signs of an acute toxæmia. Thus a general lymphoid peritonitis may be present, with the exudation of free serous fluid into the peritoneum and with flocculi of lymph on the peritoneal surface, œdema of the mesentery, enlargement and softening of the mesenteric glands. The right heart may be engorged, the liver and spleen enlarged and softened. Should the patient survive this acute stage—which he seldom does—the necrotic mucosa is exfoliated in much the same manner as a diphtheritic membrane, a condition which has given rise to the term *diphtheritic dysentery*.

When the necrotic patches have a more local distribution, irregular ulcers, often communicating with one another by submucous sinuses, form and may involve the entire bowel wall.

In a bowel which has undergone extensive destruction it is doubtful whether complete regeneration of the mucous membrane can take place; in fact, the whole process of repair would seem to constitute a struggle between proliferation of the specialized epithelium and fibrosis. Apparently general hypertrophy of the bowel wall does not occur as in amœbiasis.

Chronic ulceration of the large gut in bacillary dysentery may occur. The smallest lesions are lenticular in shape and involve the mucous surface alone. The more advanced lesions amount to ulceration of limited tracts of mucous membrane, rarely penetrating below the muscularis mucosæ. Ante-mortem perforation of the gut may supervene, though it is extremely rare. For the differentiation of these ulcers from those of amœbic dysentery the reader is referred to the Table on p. 422.

These ulcers must also be distinguished from those of tuberculous, enteric, and bilharzial origin.

Mucous retention cysts, due to the formation of pseudo-adenomata from the bases of Lieberkühn's follicles, may sometimes be found as a sequela of bacillary ulceration. They may be recognized as jelly-like elevations forcing up the mucous surface and scattered throughout the length of the large gut. Repair of these chronic ulcers would appear to take place extremely slowly; they leave behind them puckered pigmented depressions, the pigmentation being probably due to the deposition of iron sulphide.

Formation of granulation tissue.—Many cases of chronic bacillary dysentery acquired in the recent war showed no ulceration, but only a granular condition of the mucous membrane of the large gut. The lesions were distributed, as a rule, in an irregular manner; more usually confined to the lower portion of the large intestine. Considerable infiltration of the walls of the gut is associated with this condition.

The microscopic structure of the intestine in acute bacillary dysentery is illustrated in Plate XVIII., in which the colliquative necrosis of the mucosa

Digitized by Google

MICROSCOPICAL SECTION OF THE LARGE INTESTINE IN BACILLARY DYSENTERY.

Showing necrosis of the mucosa, cellular infiltration, and hæmorrhages into the submucosa. (*Manson-Bahr.*)

PLATE XVIII.

Digitized by Google

Digitized by Google

with almost indistinguishable cell elements can be seen. The submucosa is the seat of numerous capillary hæmorrhages and of round-cell infiltration. The formation of large macrophage cells from the capillary endothelium of the vessels may also be observed. Owing to their large size, hyaline appearance, and vacuolated protoplasm these cells, even in microscopic sections, are liable to be mistaken for *Entamœba histolytica*.

It is quite common to find evidences of an acute bacillary inflammation in a scarred fibrotic bowel which has successfully recovered from a previous attack; this may also occur as a terminal infection in natives suffering from chronic ulceration due to the *Entamœba* or to *Schistosoma mansoni*.

Symptoms.—The clinical symptoms of bacillary dysentery are never characteristic enough to enable one to establish a diagnosis without laboratory aid. As in every other form of acute intestinal infection, all degrees of severity, from a mild diarrhœa to an acute fulminating choleraic attack, may occur in the same epidemic.

The main clinical symptoms are those of inflammation of the great intestine, viz., griping, tenesmus, the passage of frequent, loose, scanty, muco-sanguineous stools, often with dysuria.

The illness may begin in various ways—insidiously or suddenly; with high fever, moderate pyrexia, or without any material rise of temperature; again, the symptoms may be grafted on to some general disease such as scurvy or malaria, or on to some chronic disease of the alimentary canal, as sprue. They may assume acute characters, or from the outset the symptoms may be subdued. As a general rule, the nearer to the rectum the lesions, the more urgent the tenesmus; the nearer to the cæcum, the more urgent the griping. The general constitutional symptoms due to the absorption of toxins may be very marked. Vomiting may occur from the outset or be absent altogether.

The *incubation period*, as far as is known from experiments on man, is a short one, generally from one to seven days.

Palpation of the abdomen can be effected only with difficulty during the early stages, owing to the protective rigidity of the recti. Later, especially in toxic and fatal cases, the abdomen may become quite lax and the sigmoid colon can be easily distinguished as an elastic coil under the examining hand. The implication of other portions of the large intestine can seldom be satisfactorily detected by a physical examination.

Character of the stools.—The number and character of the evacuations may vary enormously in the different types. Their number may be uncountable, and the unfortunate victim is "glued to the commode." At first they consist of extremely viscid blood-stained mucus, which has been compared to "red currant jelly" or "frog's spawn"; it is generally odourless. The characters by

Digitized by Google

which the exudation may be distinguished from the amœbic stool are given on p. 422. A few teaspoonfuls only may be passed at a time; afterwards the stools contain less blood and assume a more purulent character. Finally, the biliary pigments make their appearance, and the fæcal character of the stool may reappear.

In the most acute and fulminating forms the mucus may contain a large proportion of dark blood and resemble "meat washings." When necrosis of the mucosa has become finally established the stools may be exceedingly offensive, grey in colour, and contain much altered blood but no mucus.

On clinical grounds, bacillary dysentery may be classified under various headings, as follows:

1. *Mild or catarrhal forms.*—A common history is that for some days the patient had suffered from what was supposed to be an attack of diarrhœa. The stools, at first bilious and watery, perhaps to the number of four or five in the twenty-four hours, had latterly and by degrees become less copious and more frequent, less fæculent and more mucoid, their passage being attended by a certain amount of straining and griping.

At the same time the tongue may remain clean, and there may be no accompanying pyrexia. The whole attack may be over in a week, and the stools may not number more than twelve in the twenty-four hours. One has seen cases in which nothing more serious than the passage of a single solid motion with viscid blood-stained mucus was noted. The majority of these mild cases are due to Flexner-Y infections, and it is possible that various "acclimatization diarrhœas" are due to the same cause.

2. *Acute bacillary dysentery.*—In another type of case the onset is much more abrupt. Within a few hours of its commencement the disease may be in full swing. The stools, at first fæculent, soon consist of little save blood-stained mucus. Very shortly the desire to stool becomes increased, the griping and tenesmus being accompanied, perhaps, by most distressing dysuria. Fever, which at the outset may have been smart and preceded by rigor, subsides. The face is anxious and pinched, the cheeks are high-coloured from a toxic flush. Slight delirium and mental confusion may be added to the clinical picture. Thirst may be considerable, anorexia complete, and the tongue white or yellow coated. In a week or more the urgency of the symptoms may diminish, and the attack tapers off into a subacute or chronic condition, or it may end as abruptly as it began. (Chart 28.)

3. *Fulminating bacillary dysentery.*—The attack generally begins suddenly, it may be in the middle of the night, with chills or smart

Digitized by Google

rigor, vomiting, headache, and a rapid rise of temperature to 100° or even 104° F. Very shortly after the rigor, purging begins, the stools rapidly assuming dysenteric characters. In from two to three days up to a week or more, collapse sets in with a subnormal temperature, and the patient dies. So virulent may be the toxæmia that death may take place before dysenteric stools are emitted. The tongue is thickly coated and all the other symptoms of an acute toxæmia are present. The abdomen is sunken and acutely tender. The stools rapidly assume a liquid, offensive character, and are of a greenish or greyish hue. Towards the end no blood nor mucus may be visible in the stools, while in number they may be uncountable. Very occasionally a greenish diphtheritic membrane has been noted round the anus, on the perineum, and even on the penis.

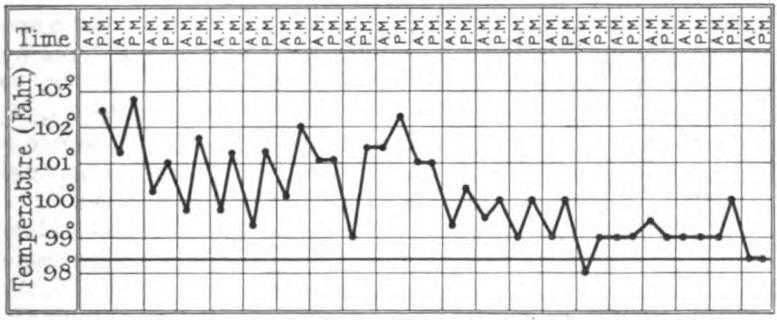


Chart 28.—Bacillary dysentery. (*Orig.*)

A *choleraic* form, in many respects resembling cholera, has been noted; these cases are by no means frequent. The onset is acute, with vomiting. Collapse with its attendant phenomena sets in early, and the stools may consist of a watery substance alternating with liquid blood-stained mucus or, it may be, almost pure serum. The temperature is subnormal, and death takes place within three days.

4. *Relapsing bacillary dysentery.*—In a proportion of bacillary dysenteries, although the urgency of the initial attack may subside, symptoms do not completely disappear. The stools may recover their fæculent character, or may even show some signs of formation, yet they continue to be passed too frequently, are often preceded by griping, and contain a variable amount of muco-pus with or without blood. Bacillary cases of this type may be due to a fresh infection or to a lighting up or recrudescence of an old focus.

Digitized by Google

5. *Chronic bacillary dysentery.*—In quite a large proportion of cases of acute dysentery the fæces do not become absolutely normal for a considerable time after the abatement of the more urgent symptoms. On the slightest indiscretion, either of food or of drink, the old symptoms reappear. In such cases sudden attacks of diarrhœa are common. For months, or even years, some patients never pass a perfectly healthy stool, the unformed motion always containing slime or muco-pus, and at times blood. Often there is a tendency to scybalous stools, or to constipation alternating with diarrhœa. Emaciation may be extreme, especially in native races, and a considerable anæmia may develop with cardiac insufficiency and dropsy. Death may ensue from exhaustion or from some intercurrent disease, such as phthisis or malaria.

Predisposing causes.—Bacillary dysentery is especially apt to attack those who are in an enfeebled state of health owing to starvation, unsuitable dietary, physical exhaustion or exposure, or whose health has been undermined and resistance lowered by some chronic disease such as malaria, tuberculosis, scurvy, or enteric. In the feeble-minded, very young children, the aged, and in pregnant women, bacillary dysentery is apt to assume a serious and toxic form. Young children may show pronounced symptoms of toxæmia, and die in convulsions or in coma.

Complications.—The commonest complication of bacillary dysentery is a mono-, or it may be a polyarthritis, which in many ways resembles rheumatoid or gonococcal arthritis. (Fig. 90.)

"*Dysenteric rheumatism,*" as it has been called, has long been known to Indian practitioners. An effusion into the cavity and ligaments surrounding the joints, especially the knee and ankle, may come on during the acute stage of the disease, or, as is more generally the case, during convalescence, when the stools are more or less fæculent. It is common in some epidemics, in others it is entirely absent. One has seen a series of cases in which arthritis was present in 27 per cent. It is most frequent in Shiga infections. A considerable pyrexia accompanies the joint-effusions. The condition may last a considerable time, but usually clears up without leaving any permanent deformity though, exceptionally, permanent disability may result. The fluid from the joints is sterile,* and will agglutinate the dysentery bacillus (Klein). This condition has to be distinguished from the fugitive serum arthritis which often occurs after the administration of anti-dysenteric serum.

Eye complications, etc.—Both acute *conjunctivitis* and *irido-*

* Shiga's bacillus has been isolated from the fluid in one instance (Elsworthy).

Digitized by Google

cyclitis are now regarded as symptomatic of dysenteric toxæmia. The former complication was commonly noted in the recent War, often associated with arthropathy, while the latter is a rare event and only occurs in a small percentage of cases. Parotitis, either unilateral or bilateral, has been noted, and is possibly due to septic absorption from the mouth. Intussusception of the large or small

Fig. 90.—Arthritis of hands and knees in bacillary dysentery.
(Photo: Dr. G. Hall.)

intestine has been found in children, and is in them a common terminal event in acute cases of the disease.

That the eye and joint complications of bacillary dysentery already described are due to an endotoxin is indicated by experimental work on animals. This shows that the filtrates of Shiga cultures when injected intravenously lead to the production of iritis and arthritis, as well as of local lesions in the cæcum.

Digitized by Google

Thrush.—As is the case in any debilitating disease, a deposit of "thrush" on the tongue and buccal mucous membrane may form and extend for some distance down the œsophagus.

The **sequelæ** of bacillary dysentery are many and varied. Destruction of the glandular tissue of the gut wall may result in stenosis or dilatation of portions of the intestinal lumen, and in various dyspeptic and obstructive troubles. Painful peristalsis owing to the formation of intestinal adhesions may be noted and may be due to peritoneal and omental bands. Disordered action and dilatation of the heart, resulting in tachycardia and irregularity, have been met with in convalescents from bacillary dysentery under active-service conditions. The liability to sprue in cases in which there is an incompletely healed lesion of the dysenteric intestine requires mention; in sprue a history of a previous and acute dysenteric attack is commonly obtainable.

Bacillary-dysentery carriers.—A carrier state supervenes in about 3 per cent. of recovered cases of bacillary dysentery. By the term "carrier" is meant a condition in which the specific bacilli continue to be excreted in an otherwise normal stool.

Carriers of the Flexner-Y bacillus are of much more frequent occurrence than are those of the Shiga bacillus. The average Flexner carrier is in good health, while the Shiga carrier is generally an invalid. The latter is naturally regarded as a danger to the community, and in all probability is suffering from a chronic ulceration of the intestinal canal. Considerable difficulty is experienced in detecting carriers, as only a small proportion can be detected by a single bacteriological examination; in all probability a much more thorough investigation is necessary. According to Fletcher, carriers are seldom encountered after the ninth month subsequent to recovery.

There is a condition in which bacillary inflammation is localized in the lower portion of the rectal canal. Persons in this condition often involuntarily pass viscid mucus, though otherwise in good health. The Editor has recently seen such a case in which Shiga's bacillus was isolated after a lapse of three years from the initial attack.

Diagnosis.—Difficulty in the diagnosis of bacillary dysentery on clinical grounds is mainly confined to the milder forms. Whenever possible a laboratory diagnosis should be made. It must not be forgotten that bacillary dysentery of a mild or chronic form occurs as a terminal infection in wasting diseases, such as phthisis, kala-azar, intestinal schistosomiasis, amœbiasis, scurvy,

Digitized by Google

and malaria. The possibility of the coexistence of enteric in cases with persistent pyrexia must not be lost sight of. In debilitated persons a *Bacillus coli* septicæmia had been frequently noted as supervening on a chronic bacillary dysentery (p. 312).

The possibility of malaria occurring in the course of bacillary dysentery should always be borne in mind. Dysenteric symptoms very often awake a latent malarial infection; this is frequently the case in the benign tertian form, and the coexistence of a primary subtertian infection with bacillary dysentery is a particularly serious combination.

Experience and attention to laboratory details and technique are necessary to ensure a rapid and correct diagnosis. For all practical purposes, in the acute stage of the disease, a simple microscopic examination of the *cellular exudate* in the stools will clinch the diagnosis—that is if, in the absence of motile amœbæ having the characters of *Entamœba histolytica*, the distinctive cellular picture is obtained. For this purpose the specimen should be brought fresh from the patient and as early as is possible in the disease. The characteristic feature of the bacillary stool as seen under the microscope (Fig. 91) is the preponderance of swollen polymorphonuclear leucocytes, with distinctive ring-like nuclei, as Willmore has recently emphasized. Excluding red blood-corpuscles, the polymorphs constitute over 90 per cent. of the total cell elements in the stool. The examination should be conducted with a $\frac{1}{6}$-in. lens and a low ocular (× 2).

Macrophage cells.—These cells, sometimes 20–30 μ in diameter, are apparently derived from a proliferation of the capillary endothelium of the gut. In shape they may be round, oval, or even bilobed. They are hyaline in appearance, and contain in their substance vacuoles and fatty granules, ingested red blood-corpuscles, or even occasionally leucocytes. They are non-motile, but, owing to their phagocytic activities, are apt to be mistaken for *Entamœba histolytica*—an error which has often been made by the inexperienced. Columnar intestinal epithelium, large mononuclear and lymphocytic cells, complete the picture. In the early stage of the disease micro-organisms visible in the mucus are few in number. Recognition of the specific dysentery bacilli cannot be effected by a simple microscopic examination.

Entamœba coli and the flagellate protozoa (*Chilomastix* and *Trichomonas*) may be present in considerable numbers in a bacillary-dysentery exudate during the convalescent stages. Much difficulty may be experienced in differentiating *E. coli* from *E. histolytica* in a bacillary-dysentery stool, and may lead to

Digitized by Google

the suspicion that one is dealing with a double infection of two diseases.

Isolation of the dysentery bacillus during life.—With practice this becomes a comparatively simple matter. The stool should be collected in a bed-pan, *which should contain no disinfectant*, and the patient should be warned against passing urine at the same time; a portion of freshly-passed blood and mucus

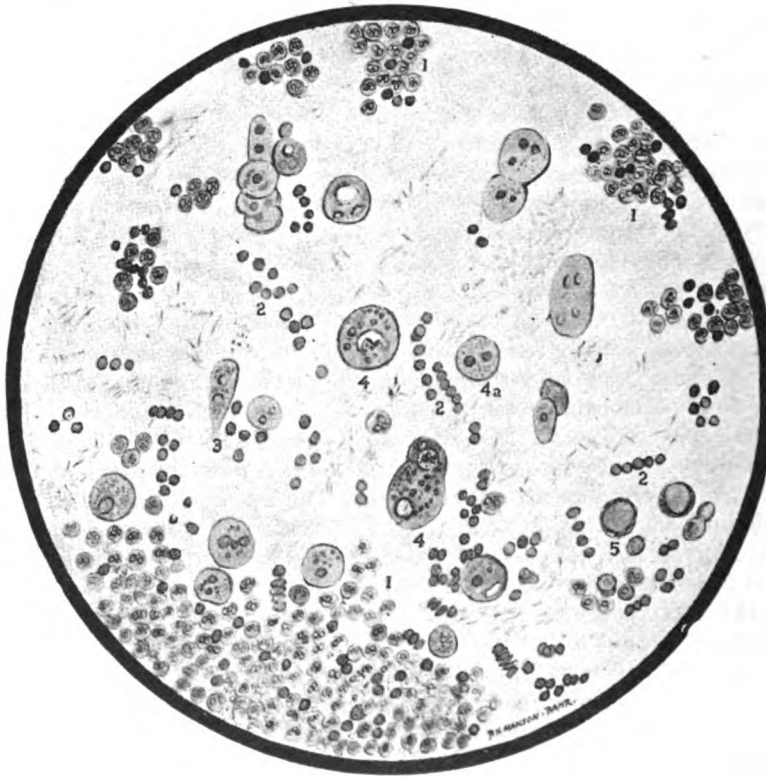


Fig. 91.—Microscopic appearances of bacillary-dysentery (Shiga) stool. (*Orig.*)

1, Polymorphonuclear pus cells; 2, red cells; 3, epithelial cells; 4, macrophage endothelial cells; 4a, macrophage containing ingested red cells liable to be mistaken for entamœbæ; 5, blastocysts.

should be picked out of the mass by means of a platinum loop, and, if soiled with fæces or urine, should be given a preliminary rinsing in distilled water or in normal saline solution. It must be remembered that the organism is very delicate and never exists in great profusion, even in a freshly-passed stool. The mucus should be spread in a spiral manner (p. 902) somewhat thickly upon a MacConkey agar plate; some prefer Conradi-Drygalski, others plain litmus-lactose agar, for this purpose. At any rate, a preliminary

Digitized by Google

incubation of the specimen in MacConkey's broth is not to be recommended, as the dysentery bacillus is so easily overgrown by other organisms of the *Bacillus coli* group.

The plate, spread in this manner, should be incubated at 37° C. in an inverted position for eighteen hours, and the small blue transparent colonies then examined with a watchmaker's lens. As a general rule, Shiga colonies are more refractile and of a more regular outline than are those of the Flexner-Y

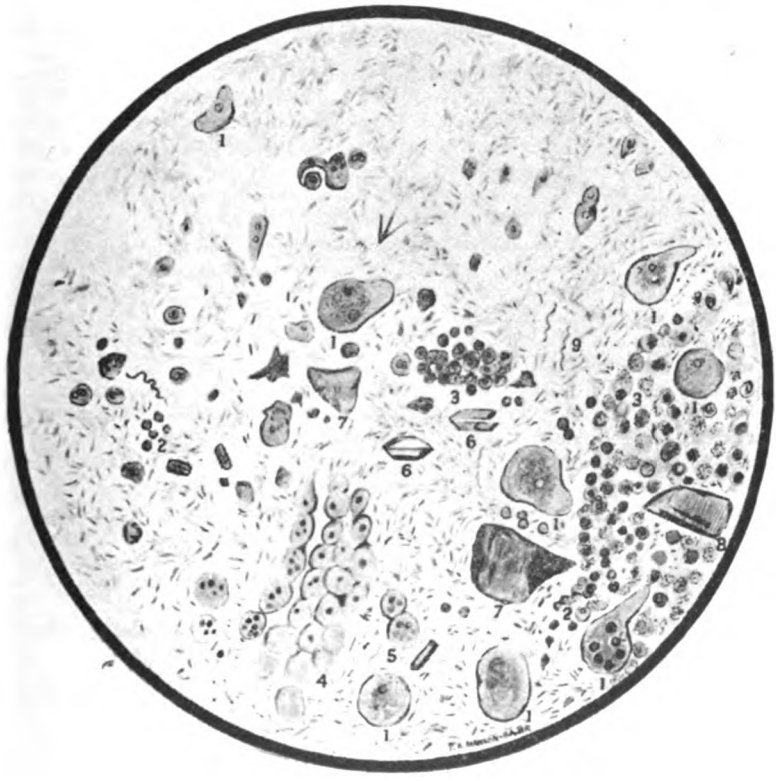


Fig. 92.—Microscopic appearances of amœbic-dysentery stool. (*Orig.*)

1, Entamœba histolytica, some containing red cells; 2, red blood-corpuscles; 3, disintegrating pus cells; 4, intestinal epithelial cells; 6, Charcot-Leyden crystals; 7, lecithin; 8, muscle-fibre; 9, spirochætes (*S. eugyratum*) and numerous bacilli.

group. In order to make their recognition still easier, it is a good plan to hold a finger or a piece of dark paper against the back of the plate.

No certain diagnosis can be made by a rough inspection of the colonies, for certain other non-lactose-fermenting organisms, *Bacillus fæcalis alkaligenes* and the *Streptococcus fæcalis*, may closely simulate colonies of the dysentery bacillus, though to the expert the colonies have an almost unmistakable appearance. It is a good plan, if any uncertainty exist, to put the plate on

Digitized by Google

the ice-chest overnight, when the characteristics of the colonies will become more pronounced.

Identification of the colonies may be carried out as follows:—Four or more should be picked off with a platinum spud and transplanted on to agar slopes, and, after a suitable incubation period, these subcultures should be emulsified and tested in high dilutions against specific anti-Shiga and anti-Flexner-Y serums in agglutination tubes. Should the method of macroscopic agglutination be utilized, these serums (as supplied by the Lister Institute) will be found very specific, so that either on a microscope slide or on the agglutinometer (p. 899) agglutination rapidly occurs.

As a measure of practical importance a method of preliminary agglutination may be employed. Ten or more suitable colonies are picked off the plate by a platinum spud or small loop, and emulsified in a very small quantity (0·25 c.c.) of normal saline; a rather thick opalescent emulsion results. By means of a capillary pipette, drops of this emulsion are placed together with an equal quantity of the specific serums diluted suitably to 1 : 50. The resulting dilution of the serums will then be 1 : 100. The test may be performed either on a microscope slide or on the agglutinometer. After oscillation for three minutes, should the reaction be positive, snowflake agglutination occurs.

After these preliminary measures the diagnosis may be confirmed by placing subcultures of the organism into the sugars (Table, p. 408).

Very occasionally the dysentery bacillus has been isolated from the bloodstream during the patient's lifetime; in the cases recorded (Ledingham and Boyd) it has proved to be the Flexner-Y bacillus. The technique is the same as for blood-culture of enteric (Appendix III., p. 895).

Isolation of the dysentery bacillus post mortem.—The bacillus can be isolated with ease from the acutely inflamed mucosa by washing the canal free from intestinal contents and scraping off the blood and mucus by means of a platinum loop. From the mucosa which has undergone coagulation necrosis this is by no means an easy matter. The surface must first be seared with a hot knife or glass and incised: the material for culture is then obtained by a platinum loop from the bottom of the incision.

The bacillus may occasionally be recovered from the inflamed mesenteric glands, but not from the bile, liver, spleen, or any solid organ.

Serological diagnosis.—The diagnosis of bacillary dysentery from the agglutinating properties of the patient's serum, on the same lines as the Widal test for enteric, has been the subject of considerable diversity of opinion. It is of little value as an aid to diagnosis in the early stages of the disease, or in the very acute or rapidly fatal types in which it is so important to arrive at an accurate opinion. Moreover, one cannot fail to be impressed with the fact that the serums of some patients, proved to be suffering from bacillary dysentery by isolation of the specific organisms from the stools, have given a negative agglutination reaction, and, further, that certain normal serums have the power of agglutinating the bacilli in low dilutions.

For the diagnosis of Shiga infection, say in convalescent or

Digitized by Google

chronic cases, an agglutination of over 1 : 25 should be obtained. It is not so much with this organism, as with the mannite-fermenting strains, that difficulties are likely to arise. This is not strange, seeing that there are apparently so many strains of the Flexner bacillus all varying in their antigenic properties, and consequently reacting solely with homologous serums. One should hesitate in cases of this description to attribute any diagnostic importance to an agglutination of under 1 : 100.

Sigmoidoscopic examination.—The sigmoidoscope is especially useful in chronic cases and should be employed wherever possible. It constitutes a valuable adjunct to laboratory diagnosis. For preparation of the patient, a simple soap-and-water enema is sufficient. The extensive employment of cathartics is not advisable, as the liquid fæces remaining in the bowel often obscure the view. The granulation tissue with surrounding hyperæmia has a characteristic appearance resembling the cortex of a granular kidney after the capsule has been stripped; at the same time infiltration and thickening of the bowel wall can be made out.

DIAGNOSIS BETWEEN BACILLARY DYSENTERY AND AMŒBIASIS

BACILLARY DYSENTERY	AMŒBIASIS
An acute disease with a tendency to epidemic spread.	A chronic endemic disease.
Incubation period a short one, 7 days or less.	Incubation period a long one, at least 20–90 days, it may be more.
Onset acute.	Onset insidious.
Pyrexia common.	Pyrexia rare, unless complicated.
Course days or weeks.	Course usually prolonged.
Complications: No hepatic symptoms; polyarthritis frequent.	*Complications:* Hepatitis, abscess of liver, more rarely in other situations.
Death due to— (*a*) Exhaustion. (*b*) Toxæmia.	Death due to— (*a*) Exhaustion. (*b*) Perforation. (*c*) Hæmorrhage. (*d*) Liver abscess.
Signs: General tenderness over whole abdomen, more marked over sigmoid flexure.	*Signs:* Local tenderness and thickening, mostly over sigmoid flexure, transverse colon, and cæcum.
Tenesmus very severe.	Tenesmus not accentuated.
Pathology: Acute diffuse necrosis of mucous membrane of large intestine, due to toxins of the dysentery bacillus.	*Pathology:* Local lesions confined solely to the large intestine, due to the characteristic ulcers.

Digitized by Google

DIAGNOSIS BETWEEN BACILLARY DYSENTERY AND AMŒBIASIS—*Cont.*

BACILLARY DYSENTERY	AMŒBIASIS
Ulcers: When present, on free edge of transverse folds of mucous membrane and distributed transversely to long axis of gut.	*Ulcers:* Commence as small abscesses of submucosa, distributed in long axis of gut.
Serpiginous in outline, with ragged undermined edges, often communicating with neighbouring ulcers; bases consist of granulation tissue.	Oval in shape, regular in outline; flask-shape in section, involving all coats; bases consist of necrotic black tenacious sloughs.
Intervening mucous membrane hyperæmic. Rarely perforate. No compensatory thickening of bowel wall.	Not uncommonly perforate; compensatory thickening of bowel wall. Intervening mucous membrane not affected.
Stools: Scanty; many in number. Bright blood-red, gelatinous, viscid mucus, odourless, resembling red-currant jelly.	*Stools:* Fæces intermingled with blood and mucus, resembling anchovy sauce. Very offensive, smelling of decomposing blood; generally copious.
Microscopic picture: Numerous red cells; polymorphs numerous, with clear-cut ring nuclei. Macrophage cells may be numerous. Few visible micro-organisms. (Fig. 91.)	*Microscopic picture:* Red cells numerous and in clumps, polymorph cells much damaged, often extruded nuclei. Macrophage cells scarce; large numbers of motile bacilli, *Entamœba histolytica*, generally with ingested red cells. Charcot-Leyden crystals common. (Acton and Thomson.) (Fig. 92.)

Prognosis depends very much upon the susceptibility and physical condition of the person attacked. In the jails of India, in fact throughout that country, though bacillary dysentery is widespread, the case-mortality is very small indeed. Of the many thousands of cases amongst British troops in the recent War, it is doubtful whether the case-mortality at any period rose above 5 per cent. Epidemics have been recorded in which the mortality was over 28 per cent., and others among debilitated natives, as for instance Solomon Islanders, in which the death-rate was 47 per cent.

Treatment.—Bacillary dysentery is, as a rule, amenable to treatment, though in its most acute form it is essential that the physician should act with energy and promptitude. The patient should be placed in bed on the appearance of the first signs, and should on no account be permitted to get up in order to pass his motions. A bed-pan should therefore be employed wherever nursing facilities are available. In the choleraic or fulminating

Digitized by Google

cases, in which the passage of stools is incessant and the physical exhaustion consequently very great, it may be advisable to dispense with a bed-pan altogether. The patient should be placed upon a waterproof sheet and the buttocks well padded with tow, which, when soiled, can be collected and burned. For this purpose the attendant, for self-protection, should wear rubber gloves.

Arrangements should be made for the periodic inspection of the stools, for by these, supplemented by the appearance of the tongue and the general condition of the patient, the progress of the case can best be estimated.

Considerable attention should be paid to the diet, which should be nutritious and easily assimilable, leaving as little residue as possible. Modern medical opinion is strongly opposed to milk in the routine treatment of bacillary dysentery. Whether plain, boiled, or peptonized, it is apt to curdle in the intestinal canal, and the casein clots thus formed have to be passed in the stools. The best diet is one consisting of jellies, albumen water, beef tea, Brand's essence, arrowroot, sago puddings, any of which may be given at two-hourly intervals in small quantities (6–10 oz.), slightly warmed, at each feed. The physical exhaustion necessitates a nutritious diet; it is therefore inadvisable to attempt to feed dysenterics over a long period on albumen water alone.

In all cases alike, even in the severest, treatment should be preceded by a mild purge; the most suitable one for the purpose is castor oil, to which tincture of opium (15 min.) may be added. The routine treatment with saline aperients has received universal commendation. The best salt for the purpose is sodium sulphate in drachm doses exhibited two-hourly for the first day or so, afterwards every four hours until the stools become fæculent.

Opium.—The routine use of opium as a means of treating the dysentery itself, and thereby immobilizing the bowel, is not to be recommended, as it is founded upon a false conception of the pathology of the disease. It is, however, permissible to exhibit opium, either by the injection of morphia or in solution, as a means of promoting sleep and easing pain, if very severe.

Bismuth.—The routine treatment by bismuth preparations has many adherents. This drug may be given in drachm doses every three hours during the early stages. The salicylate (not the subnitrate) is the preparation generally recommended.

Intestinal antiseptics.—Salol (10–15 gr.), izal, and cyllin (60–90 min.), in cachets or suspension, have been tried, apparently with good effect in some cases.

Digitized by Google

Antidysenteric serum.—Opinion is almost unanimous as to the value of an efficient antidysenteric serum in this disease. The main points are that it should be sufficiently rich in antibodies for the Shiga bacillus, and that it should be given in sufficient quantities and early in the course of the disease. The best-known serums are those prepared by the Lister Institute; similar serums are made by Mulford, the Berne Institute, by Shiga in Japan and Dopter in France. The action of the serum is to be regarded as purely antitoxic rather than antimicrobic. The idea underlying its administration is that of neutralizing the toxæmia and of preventing, if possible, cellular necrosis of the mucosa. When this has occurred, it is doubtful whether the serum has any effect whatever. Not every case of bacillary dysentery requires antiserum treatment. The indications for the injection of serum should be based upon a consideration of the patient's condition, the number of stools, the pulse, and the abdominal pain. An indication for prompt serum treatment is pyrexia, with the passage of more than twelve to eighteen stools in the twenty-four hours.

There are various routes by which the serum may be administered. In very severe or fulminating cases it is best given *intravenously* by the open method, in doses of 50–60 c.c. diluted with a pint of saline. The fluid should be injected slowly, at least ten minutes being spent in the process. It is advisable to warm the diluted serum to 99°–100° F. before injection, and, if a deposit is present, to strain it through a piece of linen which has been boiled, or through sterilized filter-paper.

Owing to the possibility of hypersensibility or anaphylaxis to horse-serum developing—which, though occurring rarely, may be attended by fatal results, especially after intravenous injection—it is advisable to inquire whether horse-serum has been administered to the patient at some previous period. In such a case one should inject a small desensitizing dose (1 c.c. with 10 c.c. saline) half an hour or so previously, and watch carefully for any untoward symptoms.

Either the median cephalic or the median basilic vein should be chosen. The veins can be made prominent by means of a rubber bandage or even by digital pressure. It is unnecessary to incise the skin. If a larger quantity has to be introduced than the syringe will hold, as is generally the case, one can disconnect the barrel, leaving the needle in the vein, and, by placing the finger gently upon the vein, exclude any air while an assistant refills the barrel.

Digitized by Google

The serum is absorbed much more quickly by the *intramuscular route* than when given subcutaneously, the time for the former being eight as against forty-eight hours. A convenient site is the adductor muscles of the thigh; the needle should be inserted at a point well external to the femoral artery. A large-bore needle should be used, and every aseptic precaution observed.

The sites generally chosen for *subcutaneous injection* are the flank, between the crest of the ilium and the costal margin, or the lax tissues over the lower part of the abdomen. The pain which results from the distension of the tissues when 100 c.c. or more are given constitutes a disadvantage to this method. Whichever route is chosen, if the toxic symptoms do not abate, a second injection may be given forty-eight hours after the first.

Care must be taken that the serum does not deteriorate after long storage. In the tropics all curative serums should be stored in the ice-chest.

A week or so after the injection, *serum sickness* is apt to supervene. An urticarial rash is accompanied by pyrexia, malaise, and stiffness of the joints. To anticipate and prevent the advent of these symptoms it is recommended that calcium lactate (20 gr.) should be given by mouth on the day of the injection, and on two or three subsequent days.

Relief of pain.—During the early stages of an attack the patient may suffer much from griping and tenesmus. These are generally relieved by hot fomentations, turpentine stupes, or by a hot bath. An excellent application is the Japanese hot-box or hand-warmer —a small tin box containing a slowly burning cartridge of powdered charcoal. These hot-boxes, or an imitation under the name of *istra*, can be procured in England. Three or four of them may be roughly sewn into a piece of flannel and laid on the abdomen. This application has the advantage of being very light, of not wetting the clothes, and of keeping warm for many hours. Tenesmus and dysuria are best relieved by morphia hypodermically; or by an enema of a wineglassful of thin starch containing 40 or 50 drops of laudanum; or by suppositories of morphia and cocaine. Washing out the rectum with a pint of very hot water, with or without boric acid, is sometimes effectual in removing for a time, or, at all events, of mitigating, the incessant desire to go to stool and to strain. Bismuth 2 dr., with laudanum 30 min. and thin starch 2 oz., is also a good sedative enema.

Collapse may occur at almost any stage, and may be due to physical exhaustion caused by excessive straining and loss of fluid. Every endeavour should be made to restore the balance

Digitized by Google

by intravenous injection of large quantities of saline; for this purpose the hypertonic solution of Rogers is to be preferred. At least two to three or even more pints of fluid should be injected. The solution should be given slowly, at a temperature of 100° F.

Vomiting and hiccough in these cases should both be regarded as being of serious portent.

Treatment of chronic bacillary dysentery cannot be considered very satisfactory, for the healing of a chronically scarred and ulcerated bowel takes place slowly and with difficulty. The diet should be carefully regulated, and small doses of aperient salines given at regular intervals. Abdominal massage over the course of the large intestine, in order to promote normal peristalsis, may assist in relieving pain and in promoting the nutrition of the gut wall.

Vaccine treatment with a mixed emulsion of Shiga's bacillus 500 millions and Flexner's bacillus 250 millions per c.c., with other micro-organisms, has been tried in East Africa in graduated doses with apparent benefit. Most authorities consider this dosage too large, and recommend as an initial dose one of 10 millions Shiga bacilli. The reaction caused by this organism may be considerable; it may be reduced by sensitizing the vaccine with anti-Shiga serum, when doses up to 200 millions can be tolerated.

Rectal injections of nitrate of silver.—A treatment which should be tried in obstinate chronic dysentery consists of injections of large quantities of nitrate-of-silver solution of a strength of ¼ to 1 gr. to the ounce of distilled water. There is a right and there is a wrong way of using this remedy. If employed in the wrong way, it is useless—perhaps worse than useless. It must never be applied when acute symptoms are present. The patient should be prepared by rest in bed and diet for a week at least. Then the bowel is to be cleared by a small dose of castor oil, followed by a large enema of 3 or 4 pints of warm water to which 2 or 3 teaspoonfuls of carbonate of soda have been added. The whole of this injection having escaped, and when the bowel is quite empty, 2 to 3 pints of the nitrate-of-silver solution are thrown in by means of a long tube passed slowly and carefully into the bowel as far as it will go without kinking. It is better to fill the bowel by gravitation, using a funnel and tube, rather than by a syringe. If it seems to be doing good, this injection may be used every few days and kept up for some time. Improvement in suitable cases generally sets in at once. The nitrate, or any other form of enema, must not be persevered with if it causes marked irritation or increase of symptoms. Protargol or argyrol, 0·5–1 per cent. in

Digitized by Google

solution, may be given in the same way. Others have used albargin 2 per cent., nargol, and collargol.

Eusol irrigation.—Latterly, lavage of the large bowel with eusol has been practised, with a considerable degree of success. The solution is made of eusol (for composition *see* p. 313) diluted one and a half times with warm water. It should be run in slowly with a tube and funnel, the patient being in the knee-elbow position. As a general rule, not more than 1½ pints can be tolerated at a time. The injections should be given on alternate days, amounting to four or six altogether. Sloughs and adherent mucus are removed by the solution, and irritation of the mucosa results. The pain thus produced becomes more intense as the treatment progresses. The sigmoidoscope should be used as a means of controlling treatment.

Other methods of treating chronic dysentery which succeed at times are the systematic washing out of the bowel daily with warm boric water, with linseed infusion, with milk (a very valuable remedy), with mangosteen-rind decoction, with weak solutions of alum, sulphate of copper or tannin 0·5 per cent., with 1 per cent. hypochlorite-of-soda solution, with creosote and water or milk—a teaspoonful to the quart; systematic daily dosing with small quantities of castor oil, with or without opium—1 to 2 drachms of castor oil with 4 to 10 drops of laudanum three times a day; 10 to 20 drops of turpentine three times a day; small doses of hydrarg. c. cretâ; the daily consumption of some preparation of fresh bael fruit; a course of Carlsbad, of Kissingen, or of Vichy water; rectal douching as practised at Plombières; a diet of grapes only, of milk only, or of beef only; cold-water compresses to the abdomen.

Surgical treatment of chronic bacillary dysentery.—When less heroic methods fail, and the patient's condition is slowly but progressively deteriorating, right inguinal colotomy offers a reasonable chance of success. If so serious an operation is declined, appendicostomy might be urged. This is easily performed and is not so risky or troublesome as colotomy. A small oblique opening is made through the abdominal wall at the spot usually selected for appendicectomy. The opening should be large enough to admit two fingers, and the appendix is hooked out; this is easy if no adhesions are present. The appendix is drawn through the wound until its base is in contact with the parietal peritoneum, and it is then fixed in this position by a stitch of fine silk or catgut passing through the meso-appendix and the adjacent cut edge of the peritoneum. The appendix is opened immediately or in

Digitized by Google

a few days' time. The cæcum and colon may now be washed out with normal saline, with or without boric acid or other bland antiseptic, or with an astringent solution, through the appendix, as frequently as desired. For this purpose a No. 8 rubber catheter with a copper stilette is employed, and a rectal tube with an outflow tube. The patient should lie on his back; should the cæcum get distended and the fluid fail to pass freely, turning him slightly to the left will restore the flow.

Cæcostomy.—In cases with a polypoid condition of the mucous membrane and incessant distressing blood-stained diarrhœa, this operation should certainly be given a trial. The results have recently been eminently successful in cases which were incurable by any medicinal means (A. L. Gregg). A Paul's tube is inserted into the cæcum and the fæces are allowed to escape through it, thereby placing the whole of the large intestine at rest. The lower bowel may be washed out daily with boric-acid solution, and the wound may be closed at some subsequent period.

Post-dysenteric constipation.—After the subsidence of dysentery, constipation and balling of the stools is by no means an uncommon event. This complication is best prevented, or met, by enemata of warm water to which a little salt—a teaspoonful to the pint—has been added, or, if the bowel is very irritable, of linseed tea or of thin rice-water. An occasional dose of castor oil, half to one teaspoonful, once or twice a week or oftener, and kept up so long as the motions are not quite healthy, is an excellent routine practice; its action may be supplemented by a glycerin suppository. A course of Carlsbad waters or Carlsbad salts often gives excellent results.

Food and clothing.—In chronic dysentery much attention should be given to clothing and food. The former should be woollen and warm. Dysenterics ought never to feel cold. Cold bathing is very dangerous for them; so are alcoholic drinks of all sorts. Food should be simple in the extreme. Beef, mutton, cheese, bread, coarse fruit or coarse vegetables, nuts, pickles, and suchlike are, as a rule, not well borne. Fruit and fine well-cooked vegetables in moderation are necessary and often beneficial. In obstinate chronic dysentery it is often a good thing to change the diet from slops to solids, from a meagre to a more liberal one. The quantity of food is as important as the quality. Chronic dysenterics should eat no more than suffices to maintain their weight. Large meals must be avoided, and food should not be taken unless there is appetite. Monotony of food should be guarded against. Wonderful results are sometimes got from a sea-voyage.

Digitized by Google

Prophylaxis.—The prophylaxis of bacillary dysentery consists principally in securing a pure water supply and in avoiding unwholesome food. In barracks, camps, lunatic asylums, and other public institutions, bacillary dysentery should be regarded as an infectious and readily communicable disease, and therefore patients suffering from mild symptoms, or even looseness of the bowels, should be isolated. General measures, as for instance in military camps, consist in the systematic incineration of fæces and the avoidance of deep latrines as being extremely insanitary and as forming extensive breeding-grounds for houseflies. In fact, a campaign against bacillary dysentery resolves itself to a great extent, as in enteric, into a campaign against the housefly.

In order to prevent the spread of bacillary dysentery in closely crowded communities, it is important to recognize, as early as is possible, all carriers of the infection and mild cases of the disease, which might otherwise escape recognition. No man who has recently suffered from bacillary dysentery should be employed either as a hospital orderly, or in any capacity in the kitchens, or on table or water duties.

Prophylactic inoculation against this form of dysentery had, until recent years, fallen into disfavour, mainly on account of the local reaction, often leading to necrosis, caused by vaccines of Shiga's bacillus. Graeme Gibson introduced a system of inoculation by which the toxic effects of the bacillus are neutralized by the addition of a potent anti-Shiga serum, resulting in an almost complete absence of reaction. The vaccine and serum are put up in twin phials, the bacillary emulsion being contained in one arm, the serum in the other. The first dose is 0·25 c.c., containing 500 million Shiga organisms mixed with 0·1 c.c. of serum; the second dose, given 10 days later, contains 1,000 million organisms with 0·2 c.c. of serum. Statistics are not yet available to show whether this method has any real protective value; at any rate, the immunity induced is probably not a very long one, certainly not over three months.

Epidemic gangrenous rectitis is a designation given to a disease among the natives of the hot swampy regions of South America, Fiji and other islands of the South Pacific. In Guiana it is known as "caribi" or "Indian sickness," and in Venezuela as "el becho." From the published descriptions it is probably, though not certainly, none other than a virulent form of bacillary dysentery.

Digitized by Google

CHAPTER XXX

THE DYSENTERIES (*Concluded*)

II.—AMŒBIC DYSENTERY AND AMŒBIASIS

Definition.—Amœbiasis is a term employed to indicate an infection with a protozoon—*Entamœba histolytica*—which, while causing ulceration in the intestinal canal, may form elsewhere metastatic foci, with the production of abscess in the liver, and more rarely in other organs. When the disease is confined solely to the intestinal canal it produces *amœbic dysentery*, which is insidious in its onset, chronic in its course, and with a marked tendency to relapse. Amœbiasis is amenable to ipecacuanha or its alkaloid—emetine.

Geographical distribution.—Amœbiasis probably occurs to a greater or lesser degree throughout the tropics and subtropics. During recent years sporadic indigenous cases have been reported from England and France. It is specially prevalent in India, Indo-China, China, and the Philippines, is common throughout North and Central Africa, and is widespread in the southern United States, South America, and the West Indies.

Epidemiology.—Amœbiasis arises sporadically without any particular seasonal prevalence. It is not known to occur in epidemic form. Although the most usual method by which it spreads from man to man cannot be said to have been definitely proved, yet there is evidence that, as in the case of bacillary dysentery, houseflies play a considerable part in its dissemination. The work of Wenyon and O'Connor, and more recently of Buxton, has shown that not only can the cysts of *E. histolytica* be demonstrated in the fæces of wild-caught flies, but that they continue to be passed by experimentally infected insects for sixteen hours or longer. There is also evidence to show that contaminated water and fresh vegetables, such as lettuces, may constitute suitable vehicles of infection.

From the susceptibility of the cysts to desiccation, it is probable that dust and sand play no part in the dissemination of this disease.

Etiology.—The discovery of amœbæ in the stools of dysentery was made by Lösch in 1873, and since that date the intestinal

Digitized by Google

amœbæ have been the object of much study. The subject has been found to be a very complex and intricate one. Originally the germ was regarded as a single organism, *Amœba coli*, but it is now recognized, mainly as a result of the work of Schaudinn, Hartmann, Wenyon, and Dobell, that several distinct amœbæ occur in the intestinal canal of man, one of which, *Entamœba histolytica*, is pathogenic, while others are harmless saprophytic species. Schaudinn originally maintained that there were two well-defined species, which he named respectively *Entamœba histolytica* and *Entamœba coli;* the latter he regarded as non-pathogenic. He considered that these two species differed in their morphology, habits, and life-history. Although more recent protozoologists have modified some of Schaudinn's views on the bionomics of *E. histolytica*, yet his conception of its etiological significance has been abundantly confirmed. As a result of the work of Wenyon, O'Connor, and Dobell, we now recognize three additional non-pathogenic species—*Endolimax nana*, *Iodamœba bütschlii*, and *Dientamœba fragilis*—saprophytic in the fæces, while a fourth, *Entamœba gingivalis*, occurs in the mouth. Neither *Entamœba histolytica* nor, indeed, any of the species enumerated has, as yet, been successfully cultivated on artificial media.

Historical.—After Lösch's original discovery, Koch, although he did not recognize their significance, found, in 1883, what were obviously amœbæ in sections of the intestines and in the walls of a liver abscess. These observations were confirmed in Egypt by Kartulis in a series of papers from 1886 onwards, in which he described amœbæ in liver-abscess pus and in secondary abscesses of the brain (1904). In America similar work was done by Osler, Councilman, and Lafleur. In 1892 Kovács produced amœbic dysentery in cats by injection of dysenteric stools; and a similar result was obtained by Kruse and Pasquale, in 1894, by injection of liver-abscess pus per rectum. Harris, in 1901, produced liver abscess in puppies by intrarectal injection of dysentery amœbæ. Quincke and Roos, as early as 1893, published a careful study of the differentiation of amœbæ on a zoological basis. Ten years later Schaudinn restudied the amœbæ and differentiated them still further, but his account of the cyst formation by a process of budding off resistant spores has since been found to be erroneous. It would appear that Hüber discovered the quadrinuclear cysts of *E. histolytica* in the same year. These cysts were rediscovered in 1907 by Viereck and Hartmann, who regarded them as belonging to a new species, *E. tetragena* or *africana*. Walker, in 1911, first showed that *E. histolytica* and *E. coli* are easily separable species, and that the cysts, when mature, contain four nuclei in the former and eight nuclei in the latter. Finally, together with Sellards, in 1913, Walker proved conclusively that man becomes infected by ingestion of the cysts of these amœbæ, and that in the case of *E. histolytica* dysenteric symptoms may be produced, while the ingestion of *E. coli* is pathogenically harmless. Walker also suggested that the cysts of *E. histolytica* could occur in men showing no symptoms of the disease. These discoveries have

Digitized by Google

since been amplified and confirmed by Darling, Wenyon, O'Connor, and Dobell, and it is to the last-named protozoologist that we owe the most recent and authoritative account of the subject in "Amœbæ Living in Man," published in 1919.

Detection of entamœbæ in stools.—The dysentery amœba is known as *Entamœba histolytica* Schaudinn, 1903, a term synonymous with the *E. dysenteriæ* of Craig and the *E. tetragena* of Viereck. When present in stools, the entamœbæ (Fig. 93) are generally easy to find. All the preparation necessary is to pick out a small fragment of stool shortly after being passed, and then to lay this on

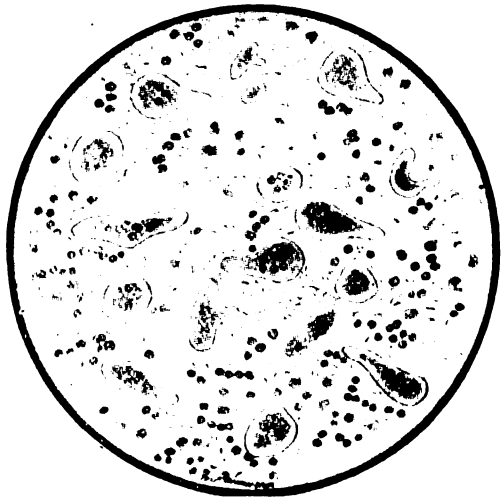


Fig. 93.—Positions assumed by active E. histolytica in stools, and characteristic cellular exudate. × 250.

the slide and compress it sufficiently under the cover-glass to form a fairly transparent film. Care should be taken that the receptacle in which the stool is collected for examination is free from all traces of antiseptics. The amœbæ live only for a few hours after being passed, and are readily distorted in the presence of urine. They are most readily found in the watery stools produced by a saline purgative, doubtless because they are washed from off the surface of the bowel by the action of the drug. In hot weather a warm stage is not required; but in cold weather it is well, until the observer has become by practice familiar with the appearance of the parasite in its passive condition, to warm the slide. This, in the absence of more elaborate apparatus, may be conveniently

Digitized by Google

dône by placing the slide on a copper or tin plate with a hole cut in it to allow transmission of light. Such a warm stage should be provided with a long arm to the end of which a spirit lamp is applied, care being taken not to raise the temperature of the slide above blood-heat. Search is then made with a $\frac{1}{6}$-in. objective. The dysentery amœba is a clear, faintly greenish-tinted, transparent body, some three to five times the diameter of a red blood-corpuscle. In its vegetative phase it is recognizable by its movenemts, which closely resemble those of the ordinary fresh-water amœba, as well as by the extraneous bodies, such as red blood-corpuscles, which it ingests. The nucleus may sometimes be detected in an excentric position. Its habit of ingesting red blood-corpuscles and body-tissue cells is one of the points of distinction between it and the non-pathogenic *E. coli*.

In stained * preparations the body of the amœba is seen to be made up of two zones—a granular endoplasm surrounded by a clear protoplasmic zone or ectoplasm. The nucleus shows a characteristic uniform structure, if the specimen is fresh and fixed while alive; aberrant forms with fragmented karyosomes, etc., are due to degeneration changes. The nucleus has a delicate achromatic membrane studded with small chromatin granules; the centre being occupied by a small spherical karyosome 0·5 μ in diameter, surrounded by an achromatic zone (Fig. 94). The space between the karyosome and the nuclear ring is occupied by a *linin* network. The endoplasm of the amœba contains numerous small granules which can be demonstrated *intra vitam* with neutral red.

The active forms show great variation in size: according to Dobell they range from 18 μ up to 40 μ in diameter; as a rule they measure between 20 μ and 30 μ. When freshly passed, amœbæ flow, rather than move, across the slide, and exhibit no very conspicuous differentiation between ectoplasm and endoplasm. They quickly die and degenerate when outside the body; if kept at a lower temperature for some time they remain stationary and eject from time to time hyaline "blade-like" pseudopodia. Degenerate amœbæ often contain vacuoles, but these are not present in healthy specimens. When conditions are adverse to the vegetative entamœba it encysts, and before doing so undergoes a reduction in size with formation of so-called precystic individuals. According to Dobell, the binucleated specimens of *E. histolytica*

* For methods of staining amœbæ in liquid preparations, *see* Schaudinn's method, Appendix III., p. 906. The details of amœbæ are distorted if attempts are made to dry the specimen as one would a blood-film.

Digitized by Google

sometimes seen in the stools are not normal division stages. He thinks that multiplication takes place in the tissues of the bowel wall, but not in the free state. It is practically certain that no process of schizogony occurs.

Cysts of E. histolytica.—These are generally much smaller (Fig. 94, 4, 5) than the vegetative forms, and provided with a definite cyst wall, 0·4 μ in thickness. They vary much in size, and, according to Dobell and Jepps, *E. histolytica* is a species which is

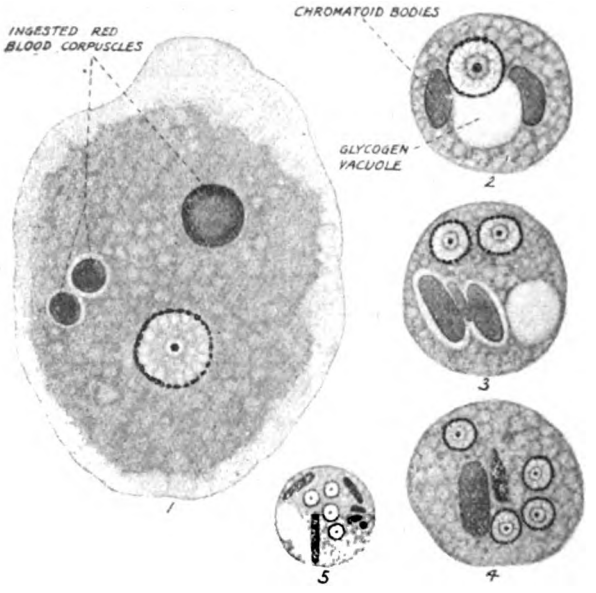


Fig. 94.—Entamœba histolytica. × 2,500 diameters. (*After Dobell.*)

1, Active amœboid form which ingested red blood-corpuscles; 2, uninucleate cyst; 3, binucleate cyst; 4, quadrinucleate cyst; 5, quadrinucleate cyst, small race, 6·6 μ in diameter.

divisible, from the size of the cysts, into five distinct races. The smallest race produce cysts 7–9 μ in diameter; the largest, 15 μ. At present there is no adequate evidence to show that these different races differ in pathogenicity. In their substance they contain highly refractile masses composed of chromatin, generally known as chromatoid bodies, which may assume the form of blocks with rounded ends. Together with these bodies a vacuole containing glycogen and staining light brown with iodine is present. When first formed the cysts contain but one nucleus, which measures about one-third of its diameter; it multiplies by binary fission

Digitized by Google

in the more mature cysts, so that finally four small nuclei, each measuring one-sixth of the diameter of the cyst, are produced. In its general characters the cyst nucleus resembles that of the vegetative stage. Freshly-passed fæces may contain cysts at any stage. The quadrinucleated cyst is considered mature, and no further nuclear division occurs in it; after a time it loses its chromatoid bodies, so that the individual cysts with well-marked inclusions may be regarded as being immature. There is not sufficient evidence that normally more than four nuclei are formed, though, according to Dobell, very rarely *E. histolytica* may have supernucleated cysts of eight.

The cysts of *E. histolytica* can only survive outside the body of man for any length of time if kept moist and cool. In water or fæces they do not live longer than a fortnight; desiccation kills them immediately, and they survive in a low much longer than in a high temperature. Degenerative changes are easily recognizable. Woodcock and Drew's observations on the excystation of *E. histolytica* seem to indicate that out of each cyst only one individual amœba emerges, and not four, as was thought previously. Dobell thinks that it is a quadrinucleate individual, which subsequently divides into uninucleate forms, but whether these conjugate in pairs after separation is still a matter of doubt.

The life-history of Entamœba histolytica can now be summarized. The active vegetative entamœbæ live on the tissues of the gut wall, where they multiply by division, and on blood-corpuscles. A certain proportion leave the ulcers they give rise to, enter the lumen of the bowel, encyst, and pass out with the fæces. The precystic individuals, free from protoplasmic inclusions, are smaller than the ordinary forms which continue to multiply in the tissues. The typical cysts, smaller than the precystic forms, are quadrinucleate when mature. When swallowed by another human host they pass into the small intestine, where they hatch into amœbulæ which in turn attack and invade the tissues and recommence the cycle.

In rare instances, however, the vegetative amœbæ may migrate from their site of election in the bowel wall and as tissue-invading forms * enter the venous system and be transported to the liver, exceptionally the spleen, brain, or lung, but by doing so they are unable to complete the cycle of development as observed outside the human body.

E. histolytica carriers.—The healthy carrier of *E. histolytica*

* Precystic individuals and cysts are found in the intestinal contents only, never in metastatic abscesses or other parts of the body.

Digitized by Google

is an individual who has not suffered or is not suffering from dysenteric symptoms, but passes *histolytica* cysts, though otherwise in perfect health. Such carriers may have active amœbæ living in their tissues.

The carriers may now be divided into two classes—(1) the *contact carrier* who has never suffered from amœbic dysentery, and (2) the *convalescent carrier* who has recovered clinically from such an attack. It is now known that for every abnormal person who is suffering from amœbic dysentery with the passage of vegetative forms which are non-infective to others, there are large numbers of healthy persons who continue to pass *E. histolytica* cysts, and thus constitute a perennials ource of infection to others. The vegetative entamœba must, in either case, live at the expense of the tissues of the host. We know from the post-mortem findings in the Philippines and elsewhere that extensive bowel ulceration can occur without visible symptoms of dysentery having been present during life, and it is a matter of common experience that liver abscess may occur in such a person. The lesions of the mucosa may even be of microscopic proportions; the probability being that only a small percentage of those infected actually show clinical evidences of amœbic dysentery. The experiments of Walker and Sellards upon man showed that out of 20 men fed with *E. histolytica*, 18 became parasitized, but only 4 developed dysenteric symptoms, though the remainder continued to pass typical cysts in their stools.

By intrarectal and intracæcal injection of fæces containing cysts into cats and puppies, ulceration of the bowel wall and even hepatic abscesses have been produced by Baetjer, Sellards, Brumpt, Wenyon, and Dobell, though it is curious that, although the fæces may be swarming with active vegetative forms, no cyst-formation has ever been observed in these animals.

The infection in carriers of *E. histolytica* is remarkably persistent, and in all probability, unless antiamœbic treatment is instituted, they continue to pass cysts for the remainder of their lives.

Incidence of carriers.—Among British soldiers after a year's service in Egypt, Wenyon and O'Connor found that there was no marked difference between carriers who had previously suffered from dysentery and those who had not (the percentages being 6·5 as against 4·5 per cent.). The carrier rate among native Egyptians, as might be surmised, was found to be considerably higher, that is 13·5 per cent. One of the most surprising outcomes of the systematic examination of fæces by protozoologists during the War has been to show the almost universal presence of the histolytica carrier. Yorke, Matthews, and Malins Smith have found a considerable percentage

Digitized by Google

of carriers among lunatics, army recruits, and the personnel of the navy in England. The two former investigators record a figure of 5 per cent.; the latter one as high as 19 per cent. The exact meaning of these figures is difficult to conjecture; they certainly do not mean that this comparatively large number of soldiers were suffering from a gross ulceration of the bowel, for we know well that indigenous *amœbic dysentery* was almost unknown among these troops at the time. Even among the insane, with a comparatively high "carrier" percentage, true amœbic dysentery is very rare Malins Smith has been able to verify the existence of only three indigenous cases in Rainhill Asylum. The same applied to the troops in France, where few indigenous cases of amœbic dysentery were reported during the War.

Pathology.—The earliest lesions of amœbic dysentery consist of minute yellow hemispherical elevations of the mucosa, which mark the site of a deeper-lying zone of necrosis. By growing in size and breaking down they form flask-shaped ulcers, the bases of which are in the submucosa. (Plate XVII., Fig. 1.) These ulcers are scattered throughout the large intestine, and never extend above the ileo-cæcal valve. The appendix may be involved.

The ulcers may not be larger than a pin's head or may enlarge to an inch or more in diameter, and as the disease progresses may become still larger. In this case the margins are rolled, the edges undermined, and the base is generally formed by the fibres of the muscular coat. The ulcers themselves are usually capped by yellowish, greenish, or even black sloughs, which may be of considerable thickness and may project into the lumen of the bowel. The lesions, as a rule, begin in the cæcum, and are scattered throughout the transverse and sigmoid colons, though the intervening mucous membrane remains healthy. When the process is a chronic one there is considerable inflammation and compensatory hypertrophy of the bowel wall. Often there may be sacculations and constrictions due to the cicatricial contractions of one part of the intestine and attenuation of another.

Thrombosis of the blood-vessels occurs at the bases of the ulcers, and often by a process of erosion an arteriole may be opened and severe or fatal hæmorrhage result. Perforation by ulcers and even massive gangrene of the gut may occur, especially in the neighbourhood of the cæcum, and lead to fatal peritonitis.

In the healed or healing gut, cicatricial pigmented scars mark the sites of the ulcers, and adhesions may form between proximal coils of intestine; these may be matted together or adherent to the liver and spleen. The intestines themselves are very friable and tear readily when handled.

In chronic cases, polypoid and, it may be, gangrenous tags hang into the lumen of the gut. The intestinal contents may

Digitized by Google

be composed of dark, almost black hæmorrhagic fæcal matter possessing a characteristic penetrating odour.

The cadavers show no signs of toxic absorption, such as occurs in the bacillary disease. Apart from wasting, the other viscera exhibit few, if any, changes.

Microscopic pathology.—It is thought that the amœbæ work their way down the crypts of Lieberkühn, multiply, and,

Fig. 95.—Section through base of amœbic ulcer, showing E. histolytica in the tissues. (*C. M. Wenyon.*)

by means of a cytolysin, disintegrate the tissues, and produce a gelatinous necrosis, with little surrounding tissue reaction, quite unlike the inflammatory changes of bacillary dysentery. (Fig. 95.) In more advanced lesions the entamœbæ may be seen lying between the muscular bundles and within the lumina of the peritoneal veins, whence they are swept as emboli into the portal vein, and lodge in the liver, so becoming the starting-point either of an amœbic hepatitis or of a liver abscess.

Digitized by Google

The superficial layers of the slough become secondarily invaded by bacteria, though the adjacent mucous membrane is comparatively healthy and shows few microscopic changes.

Symptoms.—The *incubation period* of amœbic dysentery, that is the period from the time of introduction of the cysts into the intestinal canal until the development of symptoms, is one of considerable length. An experiment of Schaudinn has a bearing on this point. Failing to induce amœbic dysentery in cats by feeding them on dysenteric fæces containing active entamœbæ, he succeeded with dried fæces which presumably contained cysts. The active, unencysted amœbæ are destroyed by the gastric juice. Walker and Sellards, by administering vegetative entamœbæ in gelatin capsules to twenty persons, succeeded in inducing the disease in four; symptoms supervened 20–95 days after ingestion of the infective material.

The great majority of cases of amœbic dysentery run a chronic course, with frequent intermissions and relapses. In fact, the capacity for latency is one of the most striking and characteristic features of amœbic dysentery. The onset is generally insidious, and the patient may complain more of diarrhœa than of dysenteric symptoms. This cannot be too much emphasized. Too often one has seen perforation leading to fatal peritonitis occur in a patient who, judged upon clinical data, was not considered to be suffering from dysentery at all. It must not be imagined that acute cases of amœbic dysentery with exacerbations of dysenteric symptoms and passage of frequent stools do not occur, but they are the exception rather then the rule.

The symptoms, both subjective and objective, are very similar to those described in bacillary dysentery; but as a rule the abdominal tenderness is much less acute, and has a definite distribution over the cæcum, where it may simulate appendicitis, and over the transverse colon, where it may simulate dyspeptic pains; more frequently it is limited to the sigmoid colon. Should ulceration occur in the rectum, tenesmus and straining, but not so pronounced as in the bacillary form, may be noted. The stools are larger than those of bacillary dysentery; they may not number more than three or four in the twenty-four hours, and they seldom exceed twelve. As a rule they contain much dark and altered blood, which imparts a penetrating and fœtid odour; in consistency and appearance they have been compared to anchovy sauce. When mucus is passed, it is streaked with blood and occurs as flecks scattered throughout the fæcal mass. Occasionally, however, the motions may be formed, and only streaked with blood and mucus,

Digitized by Google

though this most usually occurs during the more quiescent stages. Gangrenous sloughs may be passed, and even gangrene of the gut has been recorded. Unless the case is complicated by hepatitis, in which the liver is painful and definitely enlarged, there is seldom any fever, nor are there any toxic manifestations. As a rule the patient becomes progressively emaciated, though some subjects remain in remarkably good condition although suffering from repeated relapses. The tongue is moist and coated, vomiting may occur, and there is generally complete loss of appetite. Dysuria is not a prominent symptom.

Often without treatment the condition may subside, and the patient may be apparently cured, only to relapse after an interval of months, or it may be of years. More often the patient continues to pass loose, semi-formed stools, attacks of diarrhœa alternating with constipation. After any physical exhaustion, chill, alcoholic or dietetic indiscretion, a fresh exacerbation may supervene.

Death may result from exhaustion, intestinal hæmorrhage, perforation, or from liver abscess.

Perforation of the gut may be sudden, or preceded by intense local pain, which, if confined to the right iliac fossa, may be mistaken for appendicitis. The most frequent complication of amœbic dysentery is liver abscess, which will be treated separately.

Amœbiasis may be superimposed upon bacillary dysentery; this occurs more frequently than has been supposed. Visceroptosis, great distension and sacculation of the gut, leading to intractable intestinal stasis, constitute some of the most distressing sequelæ of amœbic dysentery.

Diagnosis.—Generally it is safe to regard an acutely developing, tropical diarrhœa as being of bacillary or amœbic origin. The clinical distinctions are unreliable; possibly some assistance may be obtained from the more rapid onset and pulse in the bacillary disease. As a rule the number of stools in bacillary dysentery is greater and their volume is less.

In these circumstances laboratory diagnosis should be had recourse to, the clinician having regard to the experience of the observer and his ability to determine whether any amœba-like body discovered in the fæces be *E. histolytica*, *E. coli*, or merely a large tissue cell, especially a macrophage (Fig. 91, 4a). With practice this becomes a comparatively easy matter, but it must be emphasized that the entamœbæ may be absent in some portions of a stool though numerous in others. Several preparations must be searched with the $\frac{1}{6}$-in. lens, and, whenever possible, a portion of mucus must be picked out for examination. The organ-

Digitized by Google

isms may be difficult, or almost impossible, to detect in a specimen containing much blood, and it is important that it should be as fresh as is possible. The discovery of an active amœba containing ingested red blood-corpuscles is generally sufficient to clinch a diagnosis of *E. histolytica*. In the more chronic and latent forms of the disease the characteristic cysts must be searched for; no examination should be considered to exclude completely an amœbic infection until the stool has been searched on *each of seven* consecutive days.

In cases where there is any doubt as to the identity of the cysts, the method of staining, by the rapid or by the more prolonged iron-hæmotoxylin method, may be resorted to (p. 907). Much valuable information can be obtained by mixing the fresh fæces with a solution of Weigert's iodine (p. 906), which brings out their nuclei and other characteristics.

Sigmoidoscopic examination.—In amœbic ulceration extending into the rectal canal, a sigmoidoscopic examination, which can be conducted without an anæsthetic, may afford valuable information. By means of the microscopic attachment with which the modern instruments are provided the character of the ulceration may be determined. The novice should be warned not to use this instrument freely until he has had considerable practice.

Treatment.—As in the case of bacillary dysentery, the treatment of amœbiasis, especially if acute, requires judgment and careful supervision. The rules laid down for guidance in the bacillary form should be observed. Specific drugs may be preceded by a purge—castor oil is the most appropriate; opium, as a routine measure, should be avoided. It has long been known that *ipecacuanha* is the most valuable drug in the treatment of amœbiasis. This was Manson's opinion, based on a very large experience, and bears out the popularity which this drug has long enjoyed in the treatment of chronic dysentery. It must be given on an empty stomach. The best plan is to interdict all food for three hours; then to give 10 or 20 drops of laudanum in a tablespoonful of water, and, at the same time, to apply a mustard poultice to the epigastrium. About twenty minutes later, when the patient is coming under the influence of the laudanum, 20 to 30—some give as much as 60—gr. of ipecacuanha in pill, bolus, capsule, or in suspension in about half a wineglassful of water, are administered. With a view to prevent vomiting, the patient is directed to lie flat on his back, using a low pillow, and not to eat, drink, speak, or move for at least four hours. Probably he will fall asleep. Should he feel nauseated, he must as much as

Digitized by Google

possible resist the desire to vomit. With the same object in view, when saliva begins to collect in the mouth, as it is apt to do in such circumstances, it must not be swallowed; on a slight sign from the patient the nurse should remove the accumulating saliva with a handkerchief. If much saliva be swallowed, it is sure to provoke vomiting. In some instances these precautions suffice to avert emesis. Should, however, the ipecacuanha be brought up within an hour of its being swallowed, the dose had better be repeated so soon as the nausea has subsided, the same precautions against vomiting being observed.

After six or eight hours, and when all feeling of nausea has subsided, small quantities of food may be given, and frequent and fractional feeding persisted in for six or eight hours, or until the following day, when the dose of ipecacuanha must be repeated. In many instances one or two such doses abort the dysentery, and the acute symptoms rapidly subside. It is wise, however, to go on with the ipecacuanha once or twice a day for at least a week or longer. It is a good practice to reduce the ipecacuanha by 5 gr. every day. If the drug is doing good, copious fæculent pultaceous yellow stools will be passed after a day or two. This diarrhœa, unless excessive and attended with straining or other dysenteric symptoms, must not be checked or regarded as an indication for stopping the drug.

The value of ipecacuanha in certain circumstances is still indubitable, but it has been largely superseded—wisely or not, is another matter—by its alkaloid, *emetine*, as originally advocated by Leonard Rogers. The root of Brazilian ipecacuanha (*Psychotria ipecacuanhæ*) has been found much more efficacious than the preparation from New Grenada (*Uragoya granatensis*), as it contains more emetine.

Rogers's recommendation was suggested by Vedder's work on the action of ipecacuanha on amœbæ. Working with cultures of *B. dysenteriæ*, Vedder found that solutions of ipecacuanha had no effect on cultures of that organism, but in cultures of *Amœba limax* he found that a dilution of 1 : 10,000 to 1 : 50,000 was enough to destroy them, though solutions of ipecacuanha sine emetinâ had no deleterious effect. The toxic constituent of the ipecacuanha was thus shown to be the emetine salts; they killed amœbæ in dilutions as high as 1 in 100,000. The physiological action of emetine was ascertained to be negligible; 7·5 gr. failed to produce vomiting when injected into a dog.

Altogether, there are four alkaloids of ipecacuanha—emetine, cephæline, psychotrine, and emetamine—whose exact constitution is not yet known.

It may be said that the action of emetine upon *E. histolytica* in the tissues—for it exerts no specific action at all upon other entamœbæ—is by no means settled. The careful work of Dale and Dobell has failed to confirm the original observations by Vedder and Rogers. Indeed, their experiments

Digitized by Google

show that neither emetine nor the other alkaloids of ipecacuanha exert any specific action upon *E. histolytica in vitro ;* in fact, the alkaloid psychotrine, and even quinine, which are quite inert upon *E. histolytica* in the therapeutic sense, exert a much stronger amœbicidal action *in vitro.*

All the available evidence goes to show that the judicious treatment with emetine, or ipecacuanha in one form or another, is the only measure likely to secure a radical cure. If given in insufficient dosage, or by unsuitable methods, the drug may act as a temporary remedy or palliative without effecting a radical cure. There is no evidence that it is of value in dysenteries and diarrhœas due to other causes. It should therefore not be given indiscriminately. In large doses it has a definitely toxic action. It has been proved, both by experimental evidence and by clinical observation, that if ipecacuanha, and especially emetine, be persisted with in excessive doses, it may give rise to an intractable diarrhœa (which might be considered to be due to dysentery), and may even lead to cardiac irregularity, great asthenia and collapse. It is therefore advisable that, before emetine treatment is instituted, one should make certain of the diagnosis by a thorough microscopic examination of the stool. Recently a fine, branny desquamation of the skin has been noted as a symptom of emetine poisoning.

It is advisable to begin the emetine treatment with a course of hypodermic, or intramuscular, injections of emetine hydrochloride (1 gr. in 1 c.c. of distilled water) daily for ten or twelve days. This alone does not suffice thoroughly to eradicate the infection. It is therefore necessary to supplement it by a course of emetine given by the mouth. In the tablet form it is apt to cause vomiting; it is therefore best given in ½-gr. salol-coated tablets. A more recent and more efficacious preparation of emetine, the *double iodide of emetine and bismuth* (emetine-bismuthous-iodide), containing 26 per cent. of the emetine alkaloid, should be used to supplement the hypodermic injection of emetine. This preparation is especially useful in chronic cases and in persistent carriers of *E. histolytica* cysts. The drug should be given by the mouth; there appears to be no special advantage in the intravenous injection as has been advocated. Emetine-bismuth-iodide, generally known as E.B.I., is an insoluble powder, from which the emetine is set free by contact with the intestinal juices. Experience has shown that it passes through the intestinal canal unabsorbed if compressed into a hard tablet, or if coated with an insoluble substance such as paraffin, vaseline, resin, keratin, or stearin. It is best made up in powder form in hard gelatin cachets, or mixed with

Digitized by Google

jam or syrup. The individual dose for an adult is 3 gr. of the double iodide *per diem*, and should be kept up for twelve consecutive days. The practitioner should remember that vomiting and diarrhœa are to be expected in the earlier part of the course, and are to be viewed as an indication that the drug is being absorbed. Vomiting, unless excessive, is not to be regarded as a contraindication; if no symptoms are observable, it is possible that the cachets are not being dissolved and their contents set free. It is necessary that the patient should remain in bed and partake of a liquid or wholly milk diet. The drug may be given with a cup of hot tea the last thing at night, preferably about an hour after the final meal.

Vomiting and nausea may be prevented by 10–15 min. of tinct. opii given previously. Generally slight diarrhœa is noted during a course of emetine, and most patients waste considerably while under treatment. The condition of the heart and pulse should be noted daily, but the treatment should not be discontinued unless depression becomes severe. Alcohol in any form should be prohibited.

For a *relapsing case* more than one course of treatment with emetine-bismuth-iodide may be necessary. It is now considered advisable, after the first twelve-day course, to examine the stools frequently for *E. histolytica* cysts. At least six separate examinations are necessary before a patient may be pronounced free from infection; the first one should be carried out in the first week of treatment, two more in the second, and the remainder in the third week.

In a *persistent case* the treatment should be intermitted for a week, during which time the patient may be allowed out of bed and put on a fuller diet. Then a second course of 36 gr. or even a 24-consecutive-day course of 72 gr. may be instituted.

In spite of the favourable results at first given by emetine-bismuth-iodide, one has to admit that cases resistant to this form of treatment are occurring, especially among demobilized soldiers.

Recently the Editor has had considerable success in three such cases, which had relapsed after many courses of specific treatment, by increasing the amount of E.B.I. to 4 or 5 gr. per diem when it is found to be tolerated. The dose should be split up so that 2 gr. are taken in the morning and 3 gr. at night. At the same time, intravenous injection of neo-salvarsan, as suggested by Brug, in 0·3-gr. weekly doses, appears to have a beneficial influence. Eusol rectal irrigations may also be combined with this treatment; any prominent piles should be removed.

Digitized by Google

There is much in the action of emetine which as yet is not understood. Dale and Dobell have shown that it does not produce diarrhœa or intestinal symptoms when given to normal cats, yet it completely fails to cure them if given therapeutically when they are experimentally infected with amœbic dysentery. The drug has no action on *E. coli* or other intestinal protozoa.

Patients who continue to pass cysts after such radical measures should be advised to continue with ipecacuanha pills by night —for instance, pil. ipecac. 5–10 gr.

Other drugs.—Some observers have recorded cures, in cases resistant to emetine, with the infusion of the Mexican drug "*chaparro amargosa*" (*Castela nicholsoni*—Simarubaceæ). The treatment should continue for ten days. The drug is given by the mouth and by enema. In the former method three teaspoonfuls of the powdered chaparro are boiled for half an hour in two pints of water, and cooled and strained; the tea is taken half an hour before food three times a day. This should be supplemented by enemas given about 10 A.M. and 6 P.M., in the knee-elbow position, and retained as long as is possible. Simaruba bark (*Ailanthus glandulosa*) may be given in the same manner, and in its action appears to be similar to chaparro.

Treatment of hepatitis.—The possibility of supervention of amœbic hepatitis with pyrexia and rigors should be borne in mind. During the whole course of an attack of amœbic dysentery, and for months thereafter, the condition of the liver must receive the most careful attention. We may not be able to prevent abscess of this organ; but if pain and swelling seem to suggest it, we can try by means of full and repeated doses of ipecacuanha or emetine, saline aperients, rest, low diet, fomentations, dry cupping, and similar measures to avert what, to say the least, is a very grave complication. In some cases of hepatitis ipecacuanha treatment has proved remarkably successful. It should always have a trial. Actual aspiration of the liver often has a wonderful effect in curing the hepatitis.

Prophylaxis of amœbiasis is practically the same as that already described for bacillary dysentery, and depends upon an efficient sanitation, measures directed against the housefly, which has been proved to be a carrier of the amœbic cysts, and the avoidance in the tropics of raw vegetables and other foods that may have been contaminated by human fæces. The problem of dealing with human carriers of *E. histolytica* cysts is one that is engaging the minds of sanitarians at the present time. It is not likely to arise in countries supplied with a proper system of sanitation, but in no case ought a cyst carrier to be employed as a cook or

Digitized by Google

mess orderly, or placed on water duties. Wherever possible carriers should be treated with emetine-bismuth-iodide.

Complications of Amœbiasis: Hepatic Abscess, Etc.

Definition.—Hepatic abscess is a form of suppuration in the liver, occurring especially in warm climates, principally in male Europeans and in association with amœbic dysentery.

Geographical distribution.—Abscess of the liver, of the type known as tropical abscess, for the most part a disease of warm climates, in its distribution corresponds with that of amœbic dysentery.

In Great Britain the liver abscesses met with occur most frequently in individuals who have manifestly contracted the disease in the tropics. As a disease of indigenous origin it is distinctly rare. Of course, this remark does not apply to those suppurations which are connected with ordinary pyæmia, with gall-stones, hydatids, pylephlebitis, and the like. It is apparently less common in the West Indies than in India and the East generally. In the southern hemisphere, the Cape, Transvaal, and the cooler parts of Australia, amœbic abscess is rare.

The apparent caprice in the geographical distribution of liver abscess is probably, in great part, explained by what has already been stated with regard to the distribution of amœbic dysentery, and to the effects of high atmospheric temperature and tropical habits on the European liver, together with the circumstance, as will be mentioned in the sequel, that the entamœba is the principal element in its production.

Etiology. *Relation to dysentery.*—There can be no question as to the existence of an intimate relationship between amœbic dysentery and liver abscess. Numerous and well-authenticated statistics, as well as everyday experience, attest this. In 3,680 dysentery autopsies made in various tropical countries, and collated by Woodward, 779 (21 per cent.) revealed abscesses of the liver. These figures have been abundantly confirmed since that date, and they are conclusive as to the existence of an intimate relationship between dysentery and liver abscess. It will be remembered that extensive amœbic ulceration may exist without exciting any subjective symptoms whatever. Moreover, many patients suffering from liver abscess forget, or fail to mention, the occurrence of a previous dysenteric attack, or may mislead the physician by describing such an attack as "diarrhœa."

An important point yet to be definitely settled is the exact relationship in point of time of the dysentery to the liver abscess.

Digitized by Google

In the great majority of cases the dysentery antedates the abscess, it may be by twenty years, as in a case cited by Low.

Race, sex, and climate.—Though common in Europeans in the tropics, liver abscess is rare among the natives. Thus, in the native army of India the proportion of deaths from liver abscess to the total mortality in 1894 was only 0·6 per cent., whereas in the European army it was 7·4 per cent. Man for man, the relative liability of the European soldier and the native soldier was as 95·2 to 4·8. This disproportion is in spite of the fact that the native is more liable to dysentery than the European.

It is well known that European women in the tropics, though quite as subject to dysentery as European men, rarely suffer from liver abscess; children hardly ever. It is most common between the ages of 20 and 40.

Predisposing conditions.—The foregoing considerations seem to indicate that for the production of liver abscess at least two things are necessary—a predisposing cause and an exciting cause. The *Entamœba histolytica* is certainly not always and alone both the exciting and the predisposing cause. Were this so, native soldiers and European women and children in India would suffer as frequently from liver abscess as do European males there. Some additional factor evidently complicates the problem; possibly intemperate habits and exposure lead to a special liability to hyperæmia and congestion of the liver tissue in man with a diminution in its resistance to pathological influences.

Briefly stated, the causes of liver abscess are, first, predisposing—hyperæmic and degenerative conditions of the liver; second, exciting—the *Entamœba histolytica*, or dysentery, combined with chill, dietetic excess, or traumatism.

Morbid anatomy.—It may be inferred from the symptoms that in the early stages of suppurative hepatitis there is general congestion and enlargement of the liver; in some instances this condition may be more or less confined to one lobe or even part of a lobe. Later, as we know more especially from observations in cases that have died from the attendant dysentery, one or more greyish, ill-defined, anæmic, circular patches, ½–1 in. or thereabouts in diameter, in which the lobular structure of the gland cannot be made out, are formed. These grey spots are very evident on section of the organ. A drop or two of a reddish, gummy pus may be expressed from the necrotic patches—for such they are. Still later, the centres of the patches liquefy, and distinct but ragged abscess cavities are formed. An abscess thus commenced extends partly by molecular breaking down; partly by more massive necrosis of portions of its wall; partly by the formation of additional foci of softening in the neighbourhood and subsequent breaking down of the intervening septa. The walls of such an abscess have a ragged and rotten appearance. Spherical on the whole, there may be one or more diverticula extending

Digitized by Google

from the main cavity; or contiguous abscesses may break into each other and communicate by a sinus. Occasionally a thickened blood-vessel is met with, stretching across the cavity. Though the pus and detritus lying on the abscess wall are viscid and adhesive, there is no notable exudation of lymph either lining the cavity or in the still living liver-tissue beyond. There is a peripheral zone of hyperæmia; beyond this zone the gland may appear normal or simply congested.

Number, size, and situation of abscesses.—Liver abscess may be single or multiple. If multiple, there may be two, three, or many abscesses. When single the abscess sometimes attains a great size. Frequently it is as large as a coco-nut or even larger; it has happened that the entire liver, with the exception of a narrow zone of hepatic tissue, has been converted into a huge abscess sac. When multiple the individual abscesses are generally smaller, ranging in size from a filbert to an orange.

As might be expected from considerations of the relative size of the parts, single abscess is much more common in the right than in the left and smaller lobes. What might be termed the seat of election is the upper part of the right lobe.

Adhesions to surrounding organs are frequently, though not invariably, formed as the abscess approaches the surface of the liver. In this way the danger of intraperitoneal extravasation is usually averted.

Pulmonary inflammation and abscess from escape of liver pus into the lungs are sometimes discovered post mortem. Generally the pulmonary abscess communicates with the mother abscess in the liver by a small opening in the diaphragm, the pleural sac as a whole being shut off by adhesions.

Liver pus.—The naked-eye appearance of liver pus is peculiar, and almost characteristic. When newly evacuated it is usually chocolate-coloured and streaked with, or mixed with, larger or smaller clots or streaks of blood, and here and there with streaks of clear mucoid or yellowish material. It is so thick and viscid that it will hardly soak into the dressings; it lies on the surface of the gauze like treacle on bread, spreading out between the skin and the dressing, and finding its way past the edge of the latter rather than penetrating it. When quite fresh, here and there little islands of what may be described as laudable pus may be made out in the brown mass. Sometimes it contains considerable pieces of necrotic tissue. Occasionally, from admixture of bile, the abscess contents are green-tinged. Liver purulage has always a peculiar mawkish odour; it is rarely offensive unless the abscess lie near the colon, in which case it may have a fæcal odour. Under the microscope many blood-corpuscles are discoverable, besides much broken-down liver tissue, large granular pigmented spherical cells, leucocytes, débris, oil globules, hæmatoidin crystals, and, occasionally, Charcot-Leyden crystals and entamœbæ; rarely, the ordinary pyogenic bacteria.

Amœbæ and pyogenic organisms.—The experience of tropical abscess in Egypt, India, and elsewhere is that entamœbæ may be detected in considerably over half the cases. Usually they cannot be found in freshly aspirated liver pus, or in the matter which escapes during operation, but they appear, often in great profusion, four or five days later in the discharge from the drainage-tube. In these circumstances they may occur in strings of eight or ten, an arrangement suggesting that they had developed in some tube, such as a blood- or bile-vessel. Unless the patient is treated with emetine, the amœbæ may persist in the discharge until the abscess has healed. Their appearance in the pus coming from the walls of the abscess a few days after

Digitized by Google

operation suggests that the habitat of the parasite is not so much the pus occupying the general abscess cavity as that immediately in contact with the wall and the breaking-down tissues themselves. The pus from a large proportion of cases is sterile, but occasionally one may become secondarily infected by *Bacillus coli*. Cysts of *E. histolytica* are never found.

Encystment.—In rare instances the pus of liver abscess, instead of possessing the chocolate colour and viscid consistency described above, is yellow and creamy. This is particularly the case when the abscess becomes encysted—an occasional event. The walls of these encysted abscesses are thick, smooth, resistant, and fibrous. In time their contents become cheesy, and ultimately cretified; in the latter event the cyst shrivels up and contracts to a small size.

The pathology of liver abscess was in former years a fruitful source of speculation and controversy. Much confusion has crept into the question from attempts to separate, etiologically and pathologically, multiple from single liver abscess. The former is often called "pyæmic abscess" or "dysenteric abscess," and has been set down as being the peculiar sequel of dysentery; the latter used to be considered the "tropical abscess" *par excellence*, and regarded as idiopathic and entirely unconnected with dysentery; but there can no longer be any doubt that *E. histolytica* is the etiological agent in each case, though the exact part it plays in the so-called presuppurative stage or acute hepatitis, which is curable without operation, is not yet fully understood.

Symptoms.—There is great variety in the grouping of symptoms in liver abscess. The following is a common history: The patient, after residing for some time in the tropics, enjoying good general health and living freely, was attacked with dysentery. In due course he appeared to recover, and resumed work. Several weeks or months elapsed, when, after a wetting or some such incident, he began to feel out of sorts, to suffer from headache, foul tongue, want of appetite, irregularity of the bowels, disturbed nights, excessive and unaccountable languor, irritability of temper, and depression of spirits. About the same time he began to be conscious of a sense of weight and fullness in the right hypochondrium. Later he became feverish, particularly towards evening, the oncoming of the febrile distress being sometimes preceded by a sense of chilliness. At times he had sharp stabbing pain in the right side in the region of the liver, perhaps a dry cough and, possibly, a gnawing, uncomfortable sensation or pain in the right shoulder. His friends observed that his face had become muddy and haggard. He was uneasy if he lay on his left side. The quotidian rise of temperature now became a regular feature, the thermometer every evening touching 102° F.—sometimes more, sometimes less—and sinking to near normal by morning. He now began to perspire profusely at night, and even during the day when he chanced to fall asleep. He had to change his sleeping

Digitized by Google

clothes once or even twice every night on account of the drenching sweats. (Chart 29.)

On examination it is found that the patient is somewhat emaciated; his complexion thick and muddy; his pulse 80 to 100; his tongue furred and yellowish; the palms of his hands and soles of his feet cold and clammy. As he lies on his back it is obvious, on inspection, that the epigastrium is too full for one so emaciated; and it is seen that the breathing is shallow and mainly thoracic. The right rectus muscle is rigid. Considerable discomfort, if not pain, is elicited by attempts at palpation and percussion over the right hypochondrium. The liver dullness extends an inch too high, and an inch or more beyond the costal border in the nipple line; posteriorly it rises to about the eighth rib in the line of the angle of the scapula. It is further observed that the line

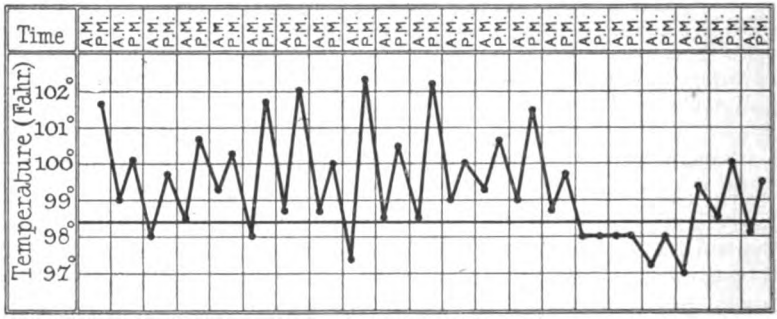


Chart 29.—Amœbic abscess of liver. (*Orig.*)

of dullness is arched along its upper border; and that it is altered by changes of position, the upper line descending when the patient lies on his left side or stands up; in the latter position the lower margin descends markedly in the epigastrium. On deep inspiration, percussion below the right costal border gives rise to much uneasiness or even to acute pain. Very likely one or two tender spots can be discovered on firm pressure being made with the finger-tips in some of the lower right intercostal spaces, or below the right costal margin. The spleen is not usually enlarged. Auscultation may detect pleuritic friction somewhere over the base of the right lung, or peritoneal friction over the liver itself. The urine, free from albumen, is scanty, high-coloured, and deposits urates. The blood shows well-marked polymorphonuclear leucocytosis, generally of 15–25 thousand, though in some abscesses, even of a large size, the leucocytosis is not pronounced.

Digitized by Google

As the case progresses, emaciation increases; hectic with drenching nocturnal sweats continues; the liver dullness and pain may further increase; or the general enlargement may somewhat subside, and percussion may reveal a pronounced local bulging, upwards or downwards. If the abscess which has now formed is not relieved by operation, after months of illness the patient may die worn out; or the abscess, which has attained enormous dimensions, may burst into the right lung or pleura, or elsewhere, and be discharged, and either recovery, or death from continued hectic and exhaustion or from some intercurrent complication, ensue.

Great variety in the urgency of symptoms.—Although the foregoing is a fairly common history in liver abscess, there are many instances in which the initial symptoms are much more urgent, and in which the disease progresses much more rapidly. In other instances subjective symptoms are almost entirely absent; or so subdued that the true nature of the case may be entirely misapprehended until the abscess bursts through the lung or bowel, or a fluctuating tumour appears in the neighbourhood of the liver; or, perhaps, not until after death, when the unsuspected abscess is discovered on the post-mortem table.

Fever.—In an acute sthenic case the initial inflammatory fever may run fairly high and persist for some time. Later, when it may be assumed that pus has formed, the fever becomes distinctly quotidian and intermittent in type, the morning temperatures being normal, or only slightly above normal, the evening rising to 101° or 102° F., or a little over or under this. Sometimes evening temperatures of 103°, rarely of 104°, are registered. In the asthenic and insidious type, at first there may be short flashes of feverishness at more considerable intervals, to be followed later by a steadier fever of a hectic type, as in the suppurative stage of the sthenic cases. In either type there may be afebrile intervals of several days' duration; and in either there may also occur, concurrently with aggravations of the local conditions, spells of continued high temperature. Occasionally, though rarely, liver abscess may be unattended by fever of any description whatever.

Rigors.—In the classical descriptions of liver abscess the occurrence of violent rigor is generally mentioned as a notable sign of the formation of pus. Undoubtedly such a rigor does at times signalize this event; but it is by no means constant, and its absence is no guarantee that abscess has not formed. Generally the evening rise of temperature is preceded by a sense of chilliness, sometimes by a more marked rigor simulating, in the regularity

Digitized by Google

of its recurrences and in its severity, the rigor of a quotidian malarial fever.

Sweating, particularly nocturnal sweating of a very profuse character, is an almost invariable accompaniment of liver abscess. The patient's clothes may be literally drenched with perspiration. Even during the day—particularly, as already mentioned, if he chance to fall asleep—the sweat may stand in beads upon the forehead and around the neck. This, like most of the other symptoms, may be temporarily absent or, in a small proportion of cases, trifling.

The *complexion* is generally muddy, cachectic and slightly icteric-looking; marked jaundice, however, is uncommon.

Wasting is generally decided and progressive.

Rheumatic-like pains and swelling of the hands and feet, such as occur in chronic septic affections, are sometimes to be noted. They usually disappear rapidly when the abscess bursts or is opened and free drainage is established.

Pain of some description is rarely absent. In a few exceptional cases there is no pain; such a patient may declare that he does not know that he has a liver.

There are several types of pain—local and sympathetic—associated with liver abscess. Complaint is almost invariably made of a sense of fullness and of a sense of weight in the region of the liver, not infrequently referred to the infrascapular region. Stabbing, stitch-like pain, increased by pressure and especially by deep inspiration, by coughing and all sudden jarring movements, is very common, and probably indicates perihepatitis from proximity of the abscess to the surface of the organ. Percussion, or firm palpation, especially if practised during deep inspiration and below the ribs in front, generally causes smart pain and decided shrinking, the rectus muscle starting up as if to protect the subjacent inflamed parts. Pain on swallowing, at the moment the bolus of food traverses the lower end of the œsophagus, has been recorded. Pain on firm pressure with the finger-tips in an intercostal space, and over a limited area, is a common and valuable localizing sign.

Pain in the right shoulder.—This symptom is present in about one-sixth of the cases, and is a reflex transmitted through the hepatic terminals of the phrenic nerve. In an abscess of the left lobe of the liver, pain is localized in the corresponding shoulder. It may be dull or acute, and in some cases it may be represented by a burning sensation, as if the surface of the skin had been flayed by a blister.

Digitized by Google

Cough of a dry, hacking character, doubtless also a reflex from irritation of the diaphragm, or from an inflamed condition of lung or pleura over the seat of abscess, is not uncommon.

Respiration is generally shallow and proportionately rapid. This is partly symptomatic of the attendant fever; oftener it is owing to the fact that fuller inspiration is attended with stitch. Sometimes the breathing is entirely thoracic, the lower part of the chest seeming to be fixed—especially the right side—and the diaphragm almost motionless.

The *decubitus* is usually dorsal or right dorsal, the body being somewhat bent towards the right side and the right leg perhaps slightly drawn up. When the patient stands, a stoop to the right may be noticeable. Lying on the left side generally causes pain from dragging on adhesions, or discomfort from the pressure of the enlarged liver on the heart and stomach. Occasionally the decubitus is indifferent, or even on the left side.

The *digestive organs* are usually disturbed and the tongue is coated. Vomiting may occur from time to time, caused either by pressure on the stomach by the swollen liver or as an expression of gastric catarrh; appetite, as a rule, is poor; flatulence may be troublesome; the bowels are confined or irregular, or there may be diarrhœa or dysentery. In the case of concurrent dysentery, it may be noted sometimes that the hepatic and dysenteric symptoms alternate in severity.

The *area of hepatic percussion dullness* is usually extended upwards and downwards, and sometimes horizontally. The extension may be general, especially in the earlier stages; later, careful outlining of the upper and lower boundaries may discover a limited and dome-like increase in one direction, most significant if upwards. The upper line of dullness is not, as a rule, horizontal, as in hydrothorax; almost invariably, on approaching the spine, it trends downwards more markedly than in hydrothorax or empyema. Variations in the extent of the dullness may take place from time to time, and sometimes very rapidly, depending not on fluctuations in the size of the liver abscess, but on the varying and relative amounts of local and general hepatic congestion. One sometimes finds even a narrow hepatic dullness in the nipple line, with a great increase in the axillary or scapular lines. In one case the lower border of the liver may be as low as the umbilicus; in another, especially in front, it may be well inside the costal margin. Diagnosis in the latter type of case is difficult, and depends rather on the nature of the fever and on the history and general condition than on local signs.

Digitized by Google

Tachycardia may be noted as a result of upward displacement of the heart by pressure of the abscess.

Splenic enlargement may be present even when there is no malarial complication. This is rare, however, and in uncomplicated cases is seldom great. Splenic tumour closely simulated by abscess of the left lobe of the liver may be encountered.

Varicosity of the epigastric and hæmorrhoidal veins—one or both—is sometimes discoverable.

Œdema of the feet and ascites are rare in the earlier stages; but the former is very usual towards the termination of long-standing cases.

Local œdema over one or more intercostal spaces, or more extensive and involving the whole or part of the hepatic area, is sometimes apparent. When limited it is a useful locating symptom.

Local bulging, if attended with fluctuation, indicates the presence of pus near the surface and the pointing of the abscess. Usually this, when it occurs, is in the epigastrium; but pus may burrow and find its way down the flank, or among the muscles of the abdominal wall, and open perhaps at a point remote from the abscess cavity in the liver.

Friction, both pleuritic and peritoneal, is sometimes to be made out, and is not without its value as a localizing symptom.

Pneumonia, generally limited to the base of the right lung, and of a subacute and persistent character, indicates contiguity of the abscess to the diaphragm. It is especially common in those cases in which the abscess subsequently ruptures through the lung. This form of chronic pneumonia is a fruitful source of error in diagnosis.

Chronological relation of the hepatitis to the dysenteric attack.—This is most irregular and uncertain. In many cases of dysentery a concurrent hepatitis is manifest almost from the commencement of the attack; this hepatitis may not subside, but pass directly to abscess-formation. Or the initial hepatitis and dysentery may both subside apparently, but the former may recur weeks, months, or even years afterwards, when, perhaps, the attack of dysentery is almost forgotten. Or there may be no active hepatic symptoms with the dysentery, hepatitis supervening only when all bowel trouble has long passed away. In a few cases no dysenteric history can be elicited; it is seldom, however, as has already been insisted on, that careful inquiry fails to bring out some story of previous bowel disturbances more or less urgent. In a few instances liver abscess of tropical origin does not declare itself

Digitized by Google

until the patient has been several years resident in a temperate climate and quite outside the endemic area.

The *incidence of the symptoms* is equally variable. Some cases commence with marked sthenic fever, much local pain, great tenderness and hepatic enlargement, the signs of suppuration, as rigor, hectic, and local bulging, rapidly supervening. Others, again, commence so insidiously that the patient can hardly say when he first began to feel ill; perhaps there may be a history of slow deterioration of the general health during a year or longer before definite hepatic symptoms show themselves. The former type seems to be the more common in the young and robust newcomer to the tropics; the latter, in the more or less cachectic and old resident. Between these extremes there is endless variety.

Duration of the disease.—Liver abscess may run its course in three weeks. Generally it is an affair of several months. Sometimes it may run on for a year or even longer; particularly so if it burst through the lung and drainage be imperfect, in which event the cavity may keep on bursting and refilling at intervals for almost an indefinite period. Occasionally a liver abscess becomes encysted and gives rise to no further symptoms, its existence being discovered only on the post-mortem table, the patient having died of quite another and independent disease.

Terminations. — Apart from operative interference, liver abscess may terminate in various ways. It may end in spontaneous rupture leading to death or recovery. Death may also be brought about in other ways—by the severity of the local disease; by prolonged hectic and exhaustion; by concurrent dysentery; or by intercurrent disease, as pneumonia, pulmonary abscess, empyema, peritonitis. Recovery may also ensue on the abscess becoming encysted or, possibly, absorbed.

Rupture of the abscess.—Rendu, in a series of 563 instances of abscess of the liver, compiled from various sources, gives an interesting table showing the direction of rupture in 159 of the cases that opened spontaneously, from which one learns that about 28 per cent. of liver abscesses rupture spontaneously, most generally into the lung or pleura.

Rupture into the lung.—If rupture take place into the lung the abscess contents may be suddenly discharged, mouthful after mouthful of pus mixed with blood welling up or being coughed up. In a few instances, in such circumstances, death has occurred suddenly from the flooding of the lungs with pus. More commonly the discharge is effected gradually, a few drachms being brought up with each cough; in the aggregate this discharge may amount

Digitized by Google

perhaps to 5 or 10 oz. in the twenty-four hours. In favourable cases the daily amount expectorated gradually diminishes until all discharge ceases and the patient recovers. Frequently, however, a deceptive arrest of discharge and cessation of cough are followed by a rise of temperature, which had become normal on the occurrence of rupture. With this there may be a reappearance of the night sweats. In a few days cough and expectoration return as before and fever once more subsides. This process of alternate emptying and refilling of the abscess cavity may recur many times before recovery finally takes place. In some cases it continues for months, and may finally wear out the patient. Abscess may form in the lung; or a sudden and fatal hæmoptysis may be brought about by ulceration opening some large pulmonary vessel. In some, expectoration never altogether ceases; if accompanied by fever this persistency indicates imperfect drainage or, possibly, the presence of a second and unruptured abscess.

Characters of the expectorated pus.—The appearance of expectorated liver-pus is almost pathognomonic. In colour it is chocolate brown; in consistence it is viscid and jelly-like. It may be streaked with blood; sometimes the expectoration may be almost entirely pure blood. Not infrequently these hæmorrhagic cases are regarded and treated as examples of ordinary hæmoptysis.

Rupture into the pleura leads to sudden development of evidences of pleural effusion, which, unless relieved by drainage, may, in its turn, give rise to all the signs of empyema, and terminate in death, or in rupture through the lung or chest wall.

Rupture into the stomach is generally signalized by vomiting of the characteristic pus and, at all events temporarily, by cessation of local symptoms and fever.

Rupture into the bowel may cause diarrhœa, the pus, more or less altered, appearing in the stool. This is an occurrence that is frequently overlooked or misinterpreted.

Rupture into the pericardium, or into a blood-vessel, is almost necessarily and rapidly fatal.

Rupture into the peritoneum is, of course, a serious occurrence, but not necessarily fatal. The majority of liver abscesses, as will be presently described, do not contain the ordinary septic bacteria, and therefore may not give rise to septic peritonitis.

Rupture through the skin is said to be the most favourable, though a rare, termination of liver abscess.

Mortality.—The case-mortality used to be considered from 50 to 80 per cent., but at the present day, owing to the introduc-

Digitized by Google

tion of emetine treatment and improved surgical technique, it is considerably less. Death may be due to pressure of the abscess upon the heart and respiratory organs, to the associated dysenteric symptoms, to rupture into the peritoneal or pleural cavity, to gangrene of the abscess wall, to pneumonia from effusion of liver pus, or to rupture into the pericardium.

Diagnosis.—Of all the grave tropical diseases, none is so frequently overlooked as abscess of the liver. Acute sthenic cases are readily enough recognized; not so the insidious asthenic cases. The novice in tropical practice is some time in realizing that grave disease of so important an organ as the liver may, for a long time, be unattended with urgent symptoms, whether local or constitutional, or both.

The most common mistakes in diagnosis are: (1) Failure to recognize the presence of disease of any description, even when an enormous abscess may occupy the liver. (2) Misinterpretation of the significance and nature of a basic pneumonia—a condition so often accompanying suppurative hepatitis. (3) Attributing the fever symptomatic of liver abscess to malaria. (4) Mistaking other diseases for abscess of the liver, and vice versa—for example, hepatitis of a non-suppurative nature, such as that attending malarial attacks; suppurative hepatitis before the formation of abscess; syphilitic disease of the liver—softening gummata which are often attended with fever of a hectic type; pylephlebitis; suppurating hydatid; gall-stone and inflammation of the gall-bladder; subphrenic abscess; abscess of the abdominal or thoracic wall; pleurisy; encysted empyema; pyelitis of the right kidney; pernicious anæmia; leucocythæmia; scurvy and similar blood diseases associated with hepatic enlargement; ulcerative endocarditis; kala-azar; undulant fever; trypanosomiasis. Any of these may be attended with fever of a hectic type, increased area of hepatic percussion dullness, and pain in or about the liver.

Many times a correct diagnosis can be arrived at only by repeated and careful study of the case in all its aspects. Golden rules in tropical practice are to think of hepatic abscess in all cases of progressive deterioration of health; and to suspect liver abscess in all obscure abdominal cases associated with evening rise of temperature, and this particularly if there be an upward enlargement of or pain in the liver, leucocytosis, and a history of dysentery—not necessarily recent dysentery. If doubt exist, there should be no hesitation in having early recourse to the aspirator to clear up diagnosis, after employing emetine or ipecacuanha as a therapeutic test.

Digitized by Google

The presence of *Entamœba histolytica* cysts in the fæces is suggestive, but by no means conclusive, of amœbic abscess.

An X-ray examination may confirm the upward enlargement of the liver and bulging of the right dome of the diaphragm which does not move on respiration.

As bearing on prognosis, apart from the risk from sudden rupture in some untoward direction, to overlook abscess of the liver is a much graver error than to mistake some other disease for liver abscess; for the chances of recovery from operation are proportionately prejudiced by every day's delay.

Low pneumonia of the right base in a tropical patient should always be regarded with suspicion; in many instances it means abscess of the subjacent liver.

Perhaps the most common error is to regard the hectic of liver abscess as attributable to *malaria*. The regularity with which the daily fevers recur, the daily chilliness or even rigor coming on about the same hour, the profuse sweating, and other circumstances so compatible with a diagnosis of malaria, all contribute to this mistake. So common is the error that Osler says he hardly ever meets with a case of liver abscess which has not been drenched with quinine. Manson's experience was the same. Medical men have made this mistake not only in their patients but in their own persons. If carefully considered, there are several circumstances which should obviate so serious an error: (1) No uncomplicated ague resists quinine in full doses. (2) In malaria, if the liver be enlarged the spleen is still more so; the reverse is the case in liver abscess. (3) The malaria parasite cannot be found in the blood in non-malarial hepatitis. (4) In liver abscess the fever is almost invariably an evening one; in malaria it most frequently comes on earlier in the day. (5) Quotidian periodicity, contrary to what is the case with tertian or quartan periodicity, is by no means pathognomonic of, or peculiar to, malaria. (6) The almost invariable history of antecedent dysentery, or at least of bowel complaint, in liver abscess. (7) Polymorphonuclear leucocytosis in liver abscess; relative mononuclear leucocytosis in malaria, kala-azar, and trypanosomiasis.

To mistake other forms of suppuration for liver abscess is of no great moment, because in many suppurative diseases the treatment is the same as for liver abscess, and no bad result need be looked for if diagnosis is not quite accurate.

A more serious error, however, is to overlook the presence of leucocythæmia, pernicious anæmia, or scurvy, and to proceed to aspirate an enlarged liver on the supposition that the symptoms

Digitized by Google

arise from abscess. Fatal intraperitoneal hæmorrhage from the puncture has been known to ensue in such circumstances. If any doubt is possible on this point, a microscopical examination of the blood should be made before proceeding to explore.

A point to note in exploring is that, when the instrument enters the liver, an up-and-down pendulum-like movement will be communicated to the outer extremity of the needle, in harmony with the rising and falling of the organ in respiration. If the needle does not exhibit this movement, its point may be in an abscess cavity, but this abscess is not in the liver.

Treatment.—Hepatitis which has not proceeded to abscess-formation should be treated, especially if dysentery be present or have been antecedent, with full doses of emetine or of ipecacuanha, repeated once or twice a day for two or three days or longer, by a cautious use of the purgative sulphates, and with poultices, rest, and low diet. Rogers has recently reiterated the value of emetine and ipecacuanha in such circumstances. If there be much pain, relief may be afforded by either wet or dry cupping over the liver, or by leeches around the anus. Ammonium chloride, 20-gr. doses three times a day, is usually prescribed.

When the occurrence of rigor, or the development of hectic, or the appearance of local bulging, or the persistency of the fever and of the local symptoms, gives ground for suspecting that abscess has formed, active medication must be suspended, a somewhat improved dietary prescribed, and measures taken without unnecessary delay to locate by means of the aspirator the position of the pus.

Aspiration.—When he uses the aspirator the surgeon must be prepared to open and drain the abscess if pus be discovered; once diagnosis is established, nothing is gained by delay. By proceeding to open the abscess at once, the shock of a double operation is avoided and only one administration of the anæsthetic is required.

To facilitate aspiration, as well as the subsequent operation if such should be found to be necessary, the patient ought invariably to be placed under an anæsthetic. Unless in very special and exceptional circumstances, it is a mistake to attempt exploration without this, for the surgeon ought to proceed with deliberation and to feel himself at liberty to make as many punctures as he may think necessary. A medium- or full-sized aspirator needle should be used, as owing to the nature of the pus it may not flow through a cannula of small bore.

If there are localizing signs, such as a tender spot, a fixed

Digitized by Google

pain, a localized œdema, localized pneumonic crepitus, pleuritic or peritoneal friction, these should be taken as indicating, with some probability, the seat of the abscess and the most promising spot for exploratory puncture. If none of these localizing signs is present, then, considering the fact that the majority of liver abscesses are situated in the upper and back part of the right lobe, the needle should, in the first instance, be inserted in the anterior axillary line in the 8th or 9th interspace, about 1 in. or 1½ in. from the costal margin and well below the limit of the pleura. The instrument should be carried in a direction inwards and slightly upwards and backwards and, if found necessary, for 3 to 3½ in. If pus be not struck the needle must be slowly withdrawn, a good vacuum being maintained the while in case the abscess has been transfixed and the point of the needle lodged in the sound tissue beyond. No pus appearing in the aspirator, the remainder of the dull hepatic area must be systematically explored, both in front and behind, regard being had to the lung and pleura on the one hand, and to the gall-bladder, large vessels, and intestine on the other. The peculiar colour—often like dirty-brown thick blood—of liver pus must not be allowed to deceive the operator into thinking that he has failed to strike the abscess.*

At least six punctures should be made before the attempt to find pus is abandoned. Provided there is complete absence of breath sounds, of vocal fremitus and resonance over the lower part of the right lung, and pus has not been reached from lower down, then the pleura or lung may be disregarded and puncture made anywhere below the line of the nipple and angle of the scapula, or wherever the physical signs suggest.

The surgeon should be encouraged to make early use of the aspirator by the fact that its employment, even where no pus is discovered, is not infrequently followed by rapid improvement in all the symptoms. Many such cases are on record. Hepatic phlebotomy, as Harley designated the removal from the liver of a few ounces of blood by the aspirator needle, is a measure of proved value in hepatitis. With due care, risk from hæmorrhage is small; it is very small indeed in comparison with the risk of allowing an hepatic abscess to remain undiscovered and unopened.

Some surgeons, in order to obviate the small risk from hæmorrhage attending aspiration through the abdominal or chest wall,

* The peculiar brownish fluid resulting from the action on blood of the carbolic lotion that had been used to sterilize the exploring syringe has been mistaken for pus. To obviate so grave a mistake the exploring syringe should be washed out with boiled water before use.

Digitized by Google

prefer to expose the surface of the liver by a short incision and then explore.

It is hardly necessary to add that strict aseptic precautions, in the way of purifying the patient's skin, the surgeon's hands, and all instruments, must be carefully observed.

Operation for abscess of the liver.—The following is the operation usually practised by English surgeons. It may be carried out either by the transperitoneal or the transpleural route.

Transperitoneal route.—If pus is struck below the costal border, the aspirator needle being left *in situ* as a guide, the abdominal wall is incised down to the peritoneum. A 3-in. incision will give plenty of room. If firm adhesions be discovered, a sinus forceps is at once run along the needle, and pushed through the intervening liver tissue and into the abscess. The aspirator cannula is now removed, and the blades of the forceps are opened sufficiently, as it is being withdrawn, to make a wound in the liver big enough to admit the forefinger, which must now be inserted and moved about so as to enlarge the wound and to gain some idea as to the size and direction of the cavity of the abscess. A rubber drainage-tube, about as large as the finger and provided with a flange, is cut to a suitable length, and carried by means of the forceps to the back of the abscess. The abscess is then allowed to empty itself. When pus no longer flows freely, a massive antiseptic dressing is applied and firmly secured by a broad binder or many-tailed bandage.

Transpleural route.—Should the abscess be struck through an intercostal space, and if the latter be not deemed sufficiently wide to admit of manipulation and free drainage, a couple of inches of rib had better be excised. The diaphragm may then be stitched to the thoracic wall, or, better, to the skin as well, when the abscess may be opened with forceps. To stitch the capsule of the liver to the diaphragm is a somewhat difficult proceeding; but if there are no reliable adhesions it had better be attempted, especially if the opening is to be made through a part of the liver covered by the peritoneum. If by any chance the pleura is opened during the operation, pneumothorax will result—an unfortunate but not necessarily a serious contingency. In this case the hole in the pleura must be carefully stitched in such a way that the pleural cavity is completely cut off before the diaphragm is divided and the abscess opened. Pus must not on any account be allowed to enter the pleural cavity; this, owing to the aspirating influence of inspiration, it would readily do if the smallest hole should remain patent.

Manson's method.—The following easy, rapid, and efficient

Digitized by Google

method of operating on abscess of the liver Manson frequently practised and recommended. The necessary apparatus (Fig. 96), which can be made by native workmen, consists of a large trocar and cannula (*a*), 4 to 5 in. long, by $\frac{3}{8}$ in. in diameter; a steel stilette (*b*) at least 14 in. in length; two metal buttons (*c*, *d*), $\frac{1}{4}$ in. at their greatest diameter, with long ($\frac{1}{2}$ in.), hollow, roughened necks into which the ends of the stilette fit loosely; 6 in. of $\frac{1}{2}$-in. stout drainage-tubing (*e*). While the ends of the drainage-tubing are held and well stretched by an assistant, they are firmly

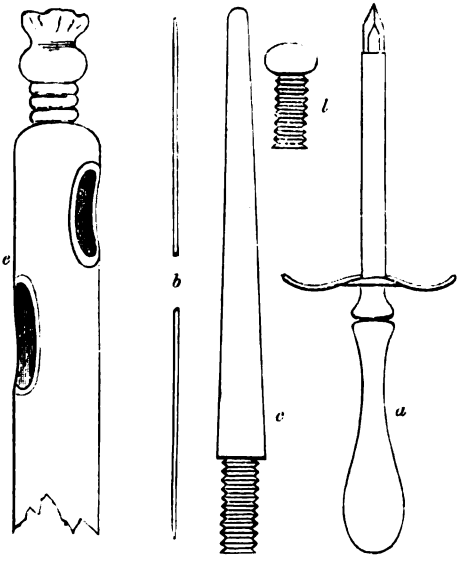


Fig. 96.—Apparatus for operation for abscess of the liver (*a* and *b* reduced).

lashed to the stem of the buttons, over the ends of the shorter (*d*) of which, for additional security, the tubing is also tied (*e*). Two large holes, to provide for free drainage, are now cut close to one end of the drainage-tube. The tube is then mounted on the stilette by inserting one end of the latter through one of the drainage holes and lodging it in the hollow neck of the distal button (*c*), and thereafter so stretching the rubber that the other end of the stilette can be inserted into the neck of the other button (*d*). When thus stretched the drainage-tube should be capable of passing easily through the cannula. The apparatus being so prepared and rendered thoroughly aseptic by soaking in carbolic

Digitized by Google

lotion, and the direction of the abscess and its depth from the surface having been carefully ascertained by means of the aspirator and noted, the aspirator is withdrawn and an incision, about 1 in. in length, made through the skin at the site of the puncture. The trocar and cannula are then thrust into the abscess and the trocar withdrawn. After allowing a small quantity of pus to escape, so as to relieve any tension that may be present in the abscess sac, the stretched drainage-tube, fenestrated end first, is slipped into the cannula and carried to the back of the abscess. Holding the drainage-tube firmly, and maintaining it carefully in contact with the back of the abscess, with one hand, the surgeon withdraws the cannula with the other. The stretched drainage-tube still firmly grasped, the button on the free end of the apparatus is slipped off the stilette, the end of which is made to perforate the drainage-tube close to the button. This it readily does, and the drainage-tube is allowed slowly to resile towards the fixed end still held in contact with the back of the abscess. When the drainage-tube has completely retracted, the stilette is withdrawn. The drainage-tube is then transfixed with a safety-pin inserted close to the skin of the abdomen, and the superfluous tubing cut off. Pus flows freely from the tube, which now firmly plugs the wound in the abdominal wall and liver, and bridges the peritoneal cavity. When the abscess has nearly emptied itself the usual massive antiseptic dressing is applied. In operating through the thoracic wall, part of a rib may, if deemed desirable, be excised before the trocar is introduced.

This operation is easily performed by the merest tyro in surgery and in the absence of skilled assistance. It may be supplemented by injecting a dilute emetine solution, 1 : 500—i.e. 3 gr. in 100 c.c. of saline.

Treatment after operation.—For the first few days after a liver abscess has been opened the discharge is considerable, and the dressing may have to be changed frequently. Very soon, however, should the case do well, the discharge rapidly diminishes, and the dressing requires renewal only every other day or every three or four days. During the first week the drainage-tube, provided it be acting efficiently, should not be disturbed, more particularly as it may be difficult to replace. Later, it may be removed and cleaned, and, when discharge has practically ceased, cautiously shortened. *It is a great mistake to begin shortening the tube before it is being pushed out, or so long as there is any appreciable discharge.* If there is the slightest indication, such as rise of temperature, that pus is being retained, the drainage must be rectified and the sinus, if necessary, dilated with forceps and finger, and a full-sized drainage-tube introduced as far as it will go. If this does not suffice, a counter-opening may have to be made. *Delay in remedying imperfect drainage is a serious, it may be fatal, error.*

Digitized by Google

Should an abscess on being opened be found to be septic, or should it become so, it must be flushed out daily, or twice a day, with a weak non-mercurial antiseptic, and a counter-opening made if necessary. Quinine solution—1 in 1,000 normal saline—is useful if much amœba-laden discharge persists for a length of time.

After liver abscess has been opened and is draining well, temperature rapidly falls, and in a few days, or almost at once, becomes normal. Should fever persist, it is to be inferred either that the drainage is inefficient, or that there are more abscesses in the liver, or that there is some complication. If it be deemed that there is another abscess, this should be sought for with the aspirator and, if found, opened and drained. Manson has seen a patient recover after three abscesses had been so treated.

It is advisable to give emetine* in grain doses hypodermically, both before and after operation, and continue it for a fortnight, whichever operation is employed.

If any symptoms of hepatic inefficiency due to extensive destruction of liver tissue are noted, the presence of diacetic acid or a high ammonia coefficient in the urine should form an indication for the oral or rectal administration of glucose and sodium bicarbonate, or in some cases for the intravenous injection of these drugs in 5- to 10-per-cent. solution.

Drainage by aspiration.—Rogers originally advocated that, for many reasons, an open operation is unnecessary, especially if surgical treatment is combined with emetine. This suggestion did not meet with favour at the time, but recent experience suggests that, wherever possible, aspiration and closure of the wound should be attempted. If the abscess is solitary and not loculated, the pus may be evacuated by means of a Potain's aspirator. The Editor has seen several cases treated on this plan with very favourable results. The shock to the patient is almost nil, and several pints of pus can be evacuated. The needle of the aspirator is directed into the abscess cavity, and negative pressure by means of the exhaust bottle is applied. After the pus has been completely evacuated, an emetine solution (3 gr. to 20 c.c. of normal saline) may be injected into the cavity, and the needle withdrawn. It is possible that after an interval the pus may reaccumulate, but it can easily be subsequently evacuated. This simple method may be tried whenever conditions are suitable.

Treatment of abscess discharging through the lung.—In the case of abscess discharging through the lung and, although emetine has been freely administered, not progressing favourably, the question of obtaining by surgical means more efficient drainage must be considered. There are two possibilities which render interference desirable: (*a*) Continued discharge of pus and blood,

* A case has been recorded of a patient who, refusing operation, was completely cured by emetine injections—21 gr. being administered altogether; of another in whom the abscess burst into the lung and all discharge ceased after the administration of emetine.

Digitized by Google

with or without attendant hectic; a condition which, if it persist, will, in all probability, in the end kill the patient. (*b*) Not infrequently prolonged discharge through the lung may induce fibrotic changes in that organ, or may give rise to pneumonia, or to abscess of the lung with all its attendant dangers, such as thrombosis or abscess of the brain. In these circumstances it is sometimes difficult to arrive at a decision as to whether an attempt should be made to open and drain the abscess, or to leave it alone. A large proportion of the cases recover, but at least an equally large number die. Of the latter, a proportion may certainly be saved by timely surgical interference.

In all cases of abscess discharging through the lung a careful register should be kept of three things—body temperature, daily amount and character of expectoration, and, once a week, the weight of the patient. If temperature keeps up, if the amount of pus continues the same or increases, or if the patient continues to lose weight, an attempt should be made at all risks to reach and drain the abscess from the outside. If temperature remains normal, if pus gradually or intermittently decreases, and if the body-weight is maintained or increases, operation is unnecessary, or, at all events, should be deferred.

In exploring the liver in such cases it must be borne in mind that most likely the abscess cavity is collapsed, and that the sides of the abscess may be in contact. Such an abscess is not likely to be discovered unless the needle be thrust in to its full extent and, whilst a good vacuum is being maintained in the aspirator, slowly withdrawn. If by good fortune the abscess has been traversed, then, when the end of the needle is crossing the cavity, a small amount of pus will be seen to flow. Great care must now be exercised to keep the needle in position so as to serve as a guide in opening the abscess. Recovery has been known to follow the introduction of a drainage-tube in the presumed direction of such an abscess, even although the abscess cavity was not entered, much less drained, by the tube.

Treatment of abscess rupturing into a serous cavity.—When there is evidence that an abscess of the liver has ruptured into the peritoneum, into the pleura, or into the pericardium, the particular serous cavity involved must be opened at once and treated on general surgical principles; otherwise the patient will almost surely die. In the circumstances the surgeon will be justified in assuming great risks.

Prognosis.—The prognosis in early operations on single abscess of the liver, provided there is no dysentery or other complication,

Digitized by Google

is good. In multiple abscess, or in single abscess if there is active dysentery or other serious complication, the prognosis is bad. In multiple abscess, if there are more than two or three abscesses, it is necessarily hopeless.

The *question of return to the tropics* after recovery from liver abscess frequently crops up. If feasible, and if the patient has not to make too great a sacrifice, he ought to remain in a temperate and healthy climate. There are many instances, however, of individuals who have enjoyed permanent good health in the tropics after recovery from liver abscess.

Amœbic abscess of the brain.—According to Armitage, 88 cases of amœbic abscess of the brain have been recorded, for the most part from Egypt. Like hepatic abscess, it is more common in men than in women. It is generally solitary, and may be regarded as a metastasis of hepatic abscess. During life it gives rise to various cerebral pressure symptoms; and it is invariably fatal.

Amœbic abscess of the spleen has been recorded.

Balantidium Dysentery

The occasional occurrence of *Balantidium coli* in the fæces, particularly in association with dysenteric diarrhœa, has been recognized for the last fifty years. It is only lately, and more particularly since Strong and Musgrave called attention to the subject, that *Balantidium coli* has come to be regarded as the germ cause of a particular type of colitis resembling in many respects amœbic dysentery. The parasite has been studied zoologically, more especially in temperate climates, but it seems probable that extended observation will show that the balantidium is equally if not more prevalent in warm climates. Cases have been reported all over the world, but especially from Germany and France; those who tend domestic pigs are exceptionally liable.

Balantidium coli is an oval-shaped ciliated infusorian measuring 0·07–0·1 mm. by 0·02–0·07 mm. Anteriorly a ciliated peristome functions as a mouth. One or more vacuoles are found in the cytoplasm. This protozoon reproduces by division, budding, and conjugation. Occasionally, losing its cilia, it may become encysted. (Fig. 97.)

How it attains the human intestine is not known, but as it is a common parasite of the pig and apes, in which it occasions a fatal form of dysentery, it is likely that one or other of these animals is the usual source of infection. As attempts to infect animals experimentally have failed, it is reasonable to conclude that the infusorian, on occasion, assumes some resistant form which enables

Digitized by Google

it to withstand the gastric and intestinal juices on the way to its habitat—the lower portion of the ileum and the large intestine. Although it may live for a considerable time in water or fæces (one hour to three days), it has not been grown on culture media. In

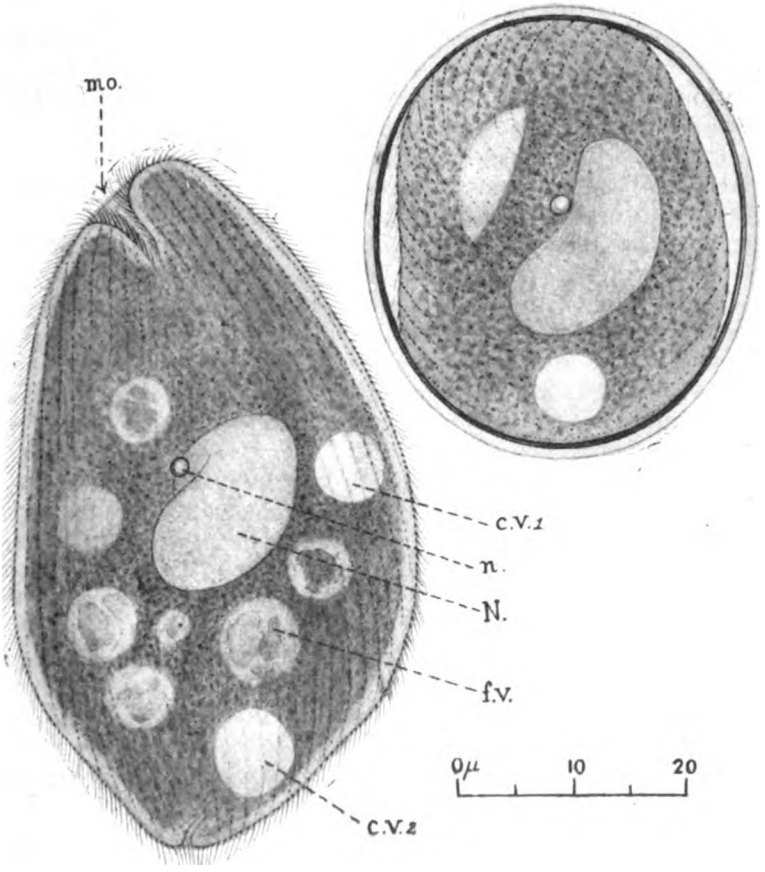


Fig. 97.—Balantidium coli. × 1,200.

(*After Dobell; by permission of Medical Research Council, Report No.* 51.)

1.—Living animal: N, meganucleus; n, micronucleus; c.v.1, anterior contractile vacuole; c.v.2, posterior contractile vacuole; f.v., food vacuole: mo., mouth.
2.—Encysted form, showing nuclei, posterior contractile vacuole, and remains of cilia.

liquid stools the balantidium exhibits great activity, indulging in locomotive as well as in rotary movements.

The symptoms of balantidium dysentery are, in the present state of knowledge, indistinguishable from those of amœbic

Digitized by Google

dysentery. The disease is chronic in type, its special nature being discoverable only on microscopic examination of the stools. Generally only one or two balantidia are found, but as many as twenty may be seen in every field of the microscope.

In the large number of cases collected from different authors by Strong, together with those observed by himself, the mortality amounted to about 30 per cent. In many cases there were no symptoms save occasional diarrhœa. How much of this was due to the parasite and how much to concurrent and independent disease it is difficult to estimate.

In 30 cases in which autopsies have been made a variety of dysenteric lesions, from catarrhal congestion and diphtheritic patches to extensive ulceration, were found. On section, Strong demonstrated the balantidium not only in exudate on the surface of the bowel, but congregated in large numbers in the follicles, and embedded in the tissues forming the base of the ulcerations, including submucosa and muscular coat, and even in the lumen of blood-vessels and lymphatics. Bowman stated that the colon may be affected throughout its whole extent with a mass of ulcers from which hang shreds of necrotic tissue—lesions resembling those of amœbic dysentery.

In the **treatment** of balantidial dysentery, Walker finds from his experimental work that organic compounds of silver are the most effective. Thymol, as in ankylostomiasis, has been recommended.

III.—VERMINOUS DYSENTERY

Bilharzial dysentery occurs in infestations with *Schistosoma mansoni*, *S. japonicum*, and more rarely with *S. hæmatobium*. It is, of course, only met with in the countries in which these parasites occur. It is due to the formation of adeno-papillomata or to actual ulceration of the large intestine, owing to the passage of numerous ova through the intestinal walls. The typical stools contain yellow or bile-stained mucus with clots or streaks of blood, in which the ova can be found under a low power of the microscope. The presence of a high eosinophilia in the blood together with symptoms of dysentery is highly suggestive, and the diagnosis should, if possible, be confirmed by the discovery of the characteristic ova in the fæces. A sigmoidoscopic examination will help in doubtful cases. In microscopic examination of the fæces for ova, the pathologist should remember that the ova are more easily found in the outer zone of solid fæces than in more fluid portions.

Digitized by Google

Infestation with Œsophagostomum apiostomum (p. 827).—This sclerostome occurs as an intestinal parasite of man in Northern Nigeria and Central Africa. When present in large numbers it gives rise to dysenteric symptoms. It has, so far, only been found in aborigines. The adult worm encysts under the submucosa, and may, together with its ova, be recognized in the dysenteric discharges.

Infestation with other helminths, such as **Ascaris, Ankylostoma duodenale,** and **Heterophyes heterophyes,** may also, though rarely, produce blood and mucus in the stools.

DIFFERENTIAL DIAGNOSIS OF THE DYSENTERIES

"**Lamblia enteritis.**"—It should be premised that, besides *E. histolytica*, *E. coli*, and *Balantidium coli*, certain other protozoa occur from time to time in the intestinal canal and appear in the fæces. Of these, perhaps *Giardia* (*Lamblia*) *intestinalis* (Fig. 98)

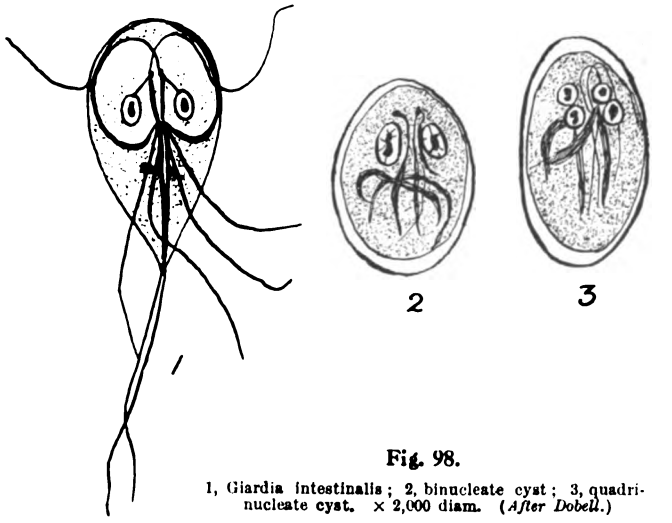


Fig. 98.

1, Giardia intestinalis; 2, binucleate cyst; 3, quadrinucleate cyst. × 2,000 diam. (*After Dobell.*)

has the best claim to be regarded as of pathological importance.* It is pear-shaped, 10 μ in length by 8 μ in breadth, and provided with twin nuclei and various flagella. The usual habitat of the parasite is the upper part of the small intestine. When newly passed in the fæces it is very active, presenting a characteristic

* Lamblia enteritis is mentioned in this section for the sake of completeness, although the diarrhœa associated with the parasite cannot strictly be classified as a dysentery.

Digitized by Google

appearance. During the passive stages the characteristic cysts appear in the fæces in enormous numbers (Fig. 98, 2, 3). It is estimated that 14,000,000,000 may be passed in a single motion. These cysts are generally found in the fæces of about 7 per cent. of normal tropical natives.

Lamblia infection is associated at times with a type of recurring diarrhœa accompanied with abdominal discomfort and the passage of bile-stained mucus—and, it may be, small amounts of blood—in which the free form of the parasite may be found in vast numbers. The stools may be of a peculiar clay colour and of a pultaceous consistency. On recovery from one of these attacks only the encysted form of the lamblia can be found. Relapses of a periodic type tend to occur, but eventually tolerance of the parasite appears to be acquired. The attack is not accompanied by emaciation, and symptoms are thought to be due to the mechanical action of the parasite, and not to an actual lesion of the mucosa; though in mice, in which these parasites cause diarrhœa, they may be found in the submucosa in sections of the gut. Lamblia infections are especially intractable, and may persist for years; many kinds of treatment have been tried without success. It has been said that bismuth salicylate, 20 gr. three times a day for a month or longer, may temporarily banish the parasite.

A note of warning should be sounded against the practice of regarding the lamblia as a cause of active disease. There are many who harbour the parasite without any inconvenience, and several authorities regard it as merely a concomitant of some other, possibly a bacillary infection.

"**Flagellate* diarrhœa.**"—*Trichomonas intestinalis* and *Chilomastix mesnili*, though occurring commonly in the fæces, have little claim to pathogenicity. They may be found in large numbers in diarrhœic fæces, and are commonly present in the convalescent stages of a bacillary dysentery.

Diarrhœa associated with Blastocystis hominis (Fig. 99).—It is necessary to mention this organism, not because it can be considered in any way pathogenic, but because it is extremely common in human fæces, especially in diarrhœic conditions in the tropics, and on account of its similarity to entamœbæ and their cysts. It is a yeast-like organism, multiplies by gemmation, and ought to be readily identified, on microscopic examination, by its irregular shape, its affinity for iodine, and the presence of iodophilic granules on the periphery of the cell.

* For a more minute description of these protozoa, as well as coccidia, occasionally seen in diarrhœic fæces, the reader is referred to pp. 768, 772.

Digitized by Google

Spirochætes in stools.—Occasionally considerable numbers of a spirochæte composed of three or more simple spirals—*Spironema eugyratum* (Fantham)—are met with in diarrhœic or dysenteric stools. Although certain authorities have credited them with pathogenic properties, there appears to be no valid reason for doing so, as they are often present in both amœbic and bacillary dysentery (Fig. 92, 9).

"Malarial dysentery."—A blood-stained discharge, or more frequently an intestinal hæmorrhage, may occur in the abdominal forms of subtertian malaria; the blood passed is very dark, due to petechial hæmorrhages into the intestinal mucosa. These are very serious cases. Instances have been recorded in which malaria was first suspected from the discovery of the parasite within the red blood-corpuscles passed per rectum. Besides the hæmorrhagic

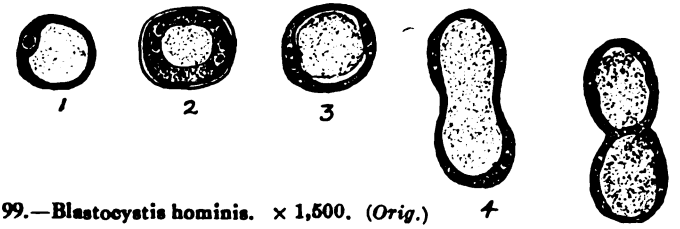


Fig. 99.—Blastocystis hominis. × 1,500. (*Orig.*)
1, 2, 3, Resting forms; 4, 5, dividing forms.

appearance of the fæces, the clinical aspect of the patient, the sweating, and the icteric tint of the sclerotics and skin, the enlarged spleen should suggest malaria.

"Kala-azar dysentery."—Blood and mucus may be passed in advanced cases of this disease. This is said to be due, not to an independent infection with the dysentery bacillus or the entamœba, but to an actual ulceration of the bowel by *Leishmania donovani*. The differentiation of this rare form of dysentery from the commoner ones should not be a matter of great difficulty.

Other conditions which may resemble dysentery.—There are other, perhaps more familiar conditions, not necessarily of tropical origin, in which dysenteric symptoms may occur. They must be briefly mentioned.

Of all familiar diseases with which dysentery of a mild form is confused, the first place must be given to *internal piles*. Of course, in this instance a correct diagnosis is readily made. Again, profuse offensive diarrhœic motions with blood and mucus may be passed in *tuberculous ulceration* of the gut. *Ulcerative colitis*, of

Digitized by Google

unknown etiology, which is frequently such a distressing disease in neurotic individuals, resembles amœbic dysentery both in its clinical features and in the character of the stools. Certain surgical conditions—*simple polypus*, stricture and *malignant* or *syphilitic disease* of the rectum, the diagnosis of which is easily settled by a simple digital examination—should be kept in mind.

Finally, it is necessary to point out that the fulminating forms of bacillary dysentery may in many cases resemble true *cholera* or *paracholera*, and that *ptomaine poisoning*, or infection with *Bacillus aertrycke* or *B. gaertner*, may in their incipient stages be very naturally confused with true bacillary or amœbic dysentery.

Digitized by Google

CHAPTER XXXI

SPRUE (PSILOSIS)

Definition.—By the term "sprue" is understood a peculiar and very dangerous form of chronic catarrhal inflammation of the whole or part of the mucous membrane of the alimentary canal, generally associated with disturbance of the chologenic function of the liver and, probably, of the functions of the other glandular organs subserving digestion. Although a disease of warm climates it may develop for the first time in temperate climates; only, however, in individuals who have previously resided in the tropics or subtropics.

Sprue is characterized by irregularly alternating periods of exacerbation and of comparative quiescence; by an inflamed, bare, and eroded condition of the mucous membrane of the tongue and mouth; by flatulent dyspepsia; by pale, phenomenally copious, and generally loose, frothy, fermenting stools; by wasting and anæmia; and by a tendency to relapse. It may occur as a primary disease, or it may supervene on other affections of the bowels. It is very slow in its progress; and, unless properly treated, tends to terminate in atrophy of the intestinal mucosa, which usually, sooner or later, proves fatal.

Nomenclature.—Sprue has been more or less recognized by writers on tropical medicine for many years. It has been called "tropical diarrhœa," "diarrhœa alba," "aphthæ tropicæ," "Ceylon sore mouth," "psilosis linguæ" (Thin), besides a variety of other names. The term "sprue" is an adaptation from the Dutch word *spruw*, in use in Java, where the disease is very common.

Geographical distribution.—It is probable that sprue, although more common in certain warm countries than in others, is found throughout the greater part of the tropical and many parts of the subtropical world. It is especially common in South China, Manila, Cochin China, Java, the Straits Settlements, Ceylon, India, the West Indies,* Southern United States, Porto Rico (Ashworth), and also occurs in Queensland. Authentic records

* Considering the frequency of pellagra in Barbadoes at the present day, it is not improbable that some of the cases of diarrhœa with sore mouth were examples of the disease originally described by Hillary in 1766.

Digitized by Google

of sprue in North and Central Africa and Arabia are rare. Apparently it is most prevalent in those tropical countries in which prolonged high temperature is combined with a moist atmosphere. It is common, however, in certain subtropical countries, as North China and even in Japan—countries where, although the summer is hot and damp, the winter is dry and bracing.

Etiology.—Prolonged residence in the endemic area is, perhaps, the most potent predisposing influence; cases, however, do occur in which the disease shows itself after a residence of one or two years only. Exhausting diseases, particularly those involving the alimentary canal, as dysentery, hill diarrhœa, morning diarrhœa, hæmorrhoids and fistula, are apt to terminate in sprue. Frequent childbearing, miscarriages, uterine hæmorrhages, exhausting discharges, and prolonged lactation also predispose to the disease; so may syphilis, courses of mercury or of iodide of potassium, bad food, bad water, anxiety, chills, and so forth —in fact, any depressing influence, particularly if it is combined with intestinal irritation. Malaria does not seem to be specially responsible.

At one time *Strongyloides intestinalis*, a parasite very common in the stools of cases of chronic intestinal flux, particularly in Cochin China, was put forward as the cause of the chronic entero-colitis (for the most part sprue) of that country. Subsequent investigations have disproved this. Like the anguillula, *Entamœba coli* may be present in the stools in these cases; but, similarly, it is in no way responsible for the disease.

Though no organism has been isolated which can with certainty be regarded as the cause of the disease, yet the yeast fungus originally described by Kohlbrügge in 1901 appears to have the best claim. The fermenting character of the stools, the gaseous dyspepsia, and the mouth lesions so reminiscent in many ways of "thrush," rather lend support to the yeast theory of the disease. During researches in Ceylon the Editor found large numbers of yeast cells in the stools as well as an infiltration of the tongue and intestinal mucus with the mycelium of this fungus. It is difficult to deny the possibility of these organisms being merely a terminal infection in such a debilitating disease. Ashford has pursued this line of investigation still further, and claims to have reproduced the disease in rabbits and guinea-pigs after intraperitoneal inoculation of yeast cultures. He considers the yeast to be a definite species peculiar to sprue and has named it *Monilia psilosis* or *Parasaccharomyces ashfordi*. It is claimed by Michel that positive complement-deviation test reactions were obtained with sprue

Digitized by Google

serums, utilizing a monilia culture as the antigen; and Martinez has recently emphasized the importance of this reaction. These latter researches still require confirmation.

Dold, in Shanghai, claims to have reproduced the clinical appearances of the disease in monkeys and mice by feeding experiments with cultures of yeasts, and to have found similar pathological appearances to human sprue at autopsy, together with an actual invasion of the intestinal mucosa by mycelium and yeast cells. He regards Ashford's claim of being able to distinguish one species of yeast as premature. His views coincide with those held by the Editor, namely, that at the present moment it is impossible to classify these organisms either by the cultural or the biochemical reactions usually employed.

Sprue has many points in common with pancreatic disease, as observed in hospital practice in temperate climates, and is possibly identical with a chronic disorder of childhood, known as Gee's cœliac diarrhœa, which may result in impairment of growth and of development. This illness, recently investigated by Still, is characterized by diarrhœa, and by profuse, pale, fermenting, and offensive stools.

Formerly sprue was supposed to be peculiar to the European in the tropics; but the Editor has shown that it is by no means rare in the descendants of the early Dutch settlers in Ceylon, and in the native Cingalese and the immigrant Tamils. Evidence has been accumulated tending to show that it is an infective disease.

There are some who believe sprue to be a food-deficiency disease, due to absence of vitamines. This view has not gained general acceptance, though the pathological changes produced by McCarrison, in his experimental monkeys fed upon a vitamine-free diet, greatly resemble the intestinal lesions of sprue.

In searching for the fundamental cause of this affection, the latency which the disease occasionally exhibits, and the fact that the first symptoms may not appear until months or even years have elapsed since the patient quitted the tropics, must be kept in view.

Symptoms. *Variability.*—There is infinite variety in the combination and in the severity of the various symptoms of sprue, as well as in the rate of progress of the disease. In some instances it may be almost a subacute process running its course in a year or two; in others, again, it may drag on intermittently for ten or fifteen years. Much depends in this respect on the circumstances, the character, the care, the treatment, the age, and the intelligence of the patient.

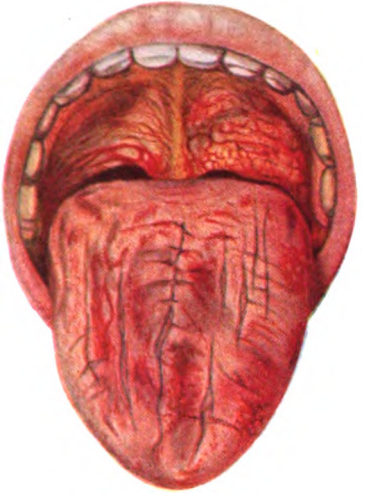
Digitized by Google

General symptoms in a typical case.—In an ordinary fully developed case the patient—who is generally dark or muddy in complexion and much emaciated—complains of three principal symptoms: soreness of the mouth, dyspeptic distension of the abdomen, looseness of the bowels; the last being particularly urgent during the early morning and part of the forenoon. The patient may also complain of feeling physically weak, of loss of memory, and of inability to take exercise or to apply his mind. His friends will probably volunteer the information that he is irritable and unreasonable.

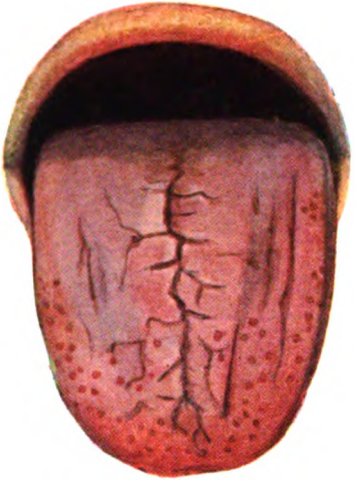
Mouth lesions.—If the mouth is examined, the soreness will be found to depend on a variety of lesions of the mucous membrane, which, though painful, seem to be of a very superficial character. These lesions vary considerably in intensity from day to day. During an exacerbation the tongue looks red and angry; superficial erosions, patches of congestion, and perhaps minute vesicles appear on its surface, particularly about the edges and tip. Sometimes, from the folding consequent on swelling of the mucous membrane, the sides of the organ have the appearance of being fissured. The filiform papillæ cannot be made out, although here and there the fungiform papillæ may stand up, pink and swollen. (Plate XIX.) If the patient be made to turn up the tip of the tongue, very likely red patches of superficial erosion, sometimes covered with an aphthous-looking pellicle, may be seen on either side of the frænum. On eversion of the lips, similar patches and erosions are visible; and if the cheek be separated from the teeth, the same may be seen on the buccal mucous membrane. Occasionally the palate is similarly affected; very often in this situation the mucous follicles are enlarged, shotty, and prominent. The gullet and uvula may also be congested and, in places, raw and sore.

In consequence of the irritation caused by these superficial and exceedingly sensitive lesions, the mouth tends to fill with a watery saliva which may dribble from the corners. If the patient attempts to take any acrid food, strong wine, or anything except the very blandest diet, the pain and burning in the mouth are intolerable; so much so that, although perhaps ravenously hungry, he shirks eating. Not infrequently swallowing is accompanied and followed by a feeling of soreness and burning under the sternum, suggesting that the gullet, like the tongue, is also in an irritated, raw, and tender condition. During exacerbations of the disease the condition of the mouth becomes greatly aggravated. Although during the temporary and occasional improvements it

Digitized by Google



Acute stage. (*After Thin.*)



Chronic stage. (*P. H. Manson-Bahr.*)

SPRUE TONGUE.

PLATE XIX.

Digitized by Google

Digitized by Google

becomes much less painful, even then salt, spices, strong wines, and all kinds of sapid foods sting unpleasantly; and the tongue, particularly along its centre, is seen to be bare and polished as if brushed over with a coating of varnish. At all times the tongue is abnormally clean and devoid of fur; during the exacerbations it is red and swollen, but during the remissions, and when not inflamed, it is small, pointed, and, owing to the anæmic condition of the patient, it may be yellowish like a piece of cartilage. Apparently the tongue condition may be the sole symptom and may persist for years before the characteristic diarrhœa supervenes.

Dyspepsia.—Dyspepsia is usually much complained of, the feelings of weight, oppression, and gaseous distension after eating being sometimes excessive. Very likely the abdomen swells out like a drum, and unpleasant borborygmi roll through the bowel. Occasionally, though not often, there may be vomiting, sometimes coming on suddenly and not always accompanied by feelings of nausea.

Anæmia may be pronounced, sometimes even in the early stages of the disease, but more generally it develops when the diarrhœa has persisted for some time. It may be very profound and may approach the pernicious type, with alteration in the size and shape of the erythrocytes and the appearance of normoblasts. It is apparently secondary to an intestinal toxæmia.

Tetany associated with dilatation of the stomach has been recorded in the terminal stages of chronic sprue.

Diarrhœa.—The diarrhœa associated with sprue is of two kinds —one chronic and habitual, the other more acute and, in the early stages, evanescent. The former is characterized by one or more daily discharges of a copious, pale, greyish, pasty, fermenting, acid, mawkish, evil-smelling material. The latter is of a watery character, also pale and fermenting, the dejecta containing undigested food and, usually, an abnormally large amount of oil and fatty acids. In these latter circumstances the diarrhœa usually brings with it considerable relief to the dyspeptic distension, at all events for a time. When the mouth is inflamed the diarrhœa is usually more active. The stools during periods of quiescence may be confined to one or two in the early morning or forenoon; during the later part of the day the patient is not disturbed. The stools, however, even in this quiescent phase, are always extraordinarily copious, the excessive bulk being attributable in great measure to the aforementioned excess of fat and to the innumerable microscopic gas bubbles; patients remark their phenomenal abundance. They are passed almost, or

Digitized by Google

altogether, without pain. Not infrequently during exacerbations there may be a tender, excoriated condition of the anus, and sometimes, in women, a similar condition of the vagina.

Types, history, course, and termination. *Protopathic sprue.*—There is a striking uniformity in the history of most cases of sprue. On inquiry, we shall probably learn that the patient has been suffering for months, or perhaps years, from irregularity of the bowels. This, we may be told, began soon after arrival in the tropics as a bilious morning diarrhœa. For a long time this morning diarrhœa went on, without interfering in any way with the general health. Later the mouth, now and again, became tender, little blisters or excoriations appearing for a day or two at a time about the tip of the tongue or inside the lips. These sore spots would come and go. Perhaps, from time to time, exacerbations of the mouth symptoms would be associated with a little increase of diarrhœa. Gradually the stools lost their bilious character and became pale and frothy; dyspeptic symptoms, particularly distension after meals, now appeared. As time went on, these symptoms would recur more frequently and in a more pronounced form, following, almost inevitably, any little imprudence as regards food or exposure. The general condition now began to deteriorate; emaciation, languor, lassitude, and inability to get through the day's work satisfactorily becoming more pronounced each summer until, finally, a condition of permanent invalidism was established. Should the disease continue to progress, the emaciation advances slowly but surely. Diarrhœa may be almost constant, and now no longer confined to the morning hours; the complexion becomes dark, sometimes very dark; the appetite, sometimes in abeyance, is more frequently ravenous, unusual indulgence in food being followed by increased discomfort, temporarily relieved by smart diarrhœa. At length the patient is confined to the house, perhaps to bed. The feet become œdematous, and the integuments hang like an ill-fitting garment, the details of the bony anatomy showing distinctly through the dry, scurfy, earthy skin. Finally, the patient dies in a semi-choleraic attack; or from inanition; or from some intercurrent disease. Such is the history of an ordinary, mismanaged case of sprue.

Sprue secondary to dysentery.—When the disease has supervened on dysentery, we learn that the motions characteristic of the original dysenteric attack had gradually changed in character; from being scanty, mucoid, bloody, and accompanied with pain and tenesmus, they became diarrhœic, pale, frothy, their discharge being followed by a feeling of relief rather than of pain. The

Digitized by Google

mouth at the same time became sore, exhibiting the characters already described. Gradually a condition of confirmed sprue was established, which ultimately, unless properly treated, will almost certainly prove fatal.

Sprue secondary to acute entero-colitis.—Another type of case commences as an acute entero-colitis with sudden and profuse colicky diarrhœa, vomiting perhaps, and a certain amount of fever. The acute symptoms do not subside completely, but gradually have the typical symptoms of sprue grafted on to those of an acute intestinal catarrh.

Incomplete sprue. (*a*) *Gastric cases.*—Occasionally we meet with cases of confirmed sprue in which, at first, the morbid process, judging from the existing clinical symptoms and subsequent history, is confined to a limited part of the alimentary canal. Thus we sometimes get sprue without diarrhœa, the principal symptoms being sore mouth, dyspeptic distension, pale copious but solid stools, and wasting.

(*b*) *Intestinal cases.*—On the other hand, we may get cases in which the mouth is not eroded and there is little or no distension or dyspepsia, but in which the stools are liquid, copious, pale, and frothy. Sometimes a patient, who may have suffered at an earlier period or on a former occasion from the first type of the disease, later acquires the diarrhœic form; and vice versa.

(*c*) *Sprue without diarrhœa.*—It sometimes happens that under treatment the sore mouth, the dyspepsia, and the diarrhœa completely subside; nevertheless the wasting continues, the stools remaining phenomenally copious—so much so that the patient may declare that more is passed than has been eaten. In this case wasting is progressive, and the patient gradually dies of inanition.

(*d*) *Mouth sprue.*—Finally, there are cases with tongue symptoms alone which may persist for many years. Whether diarrhœa may ultimately develop is not known.

Intestinal atrophy consequent on sprue.—In certain instances, under treatment the symptoms proper to sprue subside; but the patient's digestive and assimilative faculties are permanently impaired. Slight irregularities either in the quality or the amount of food, chill, fatigue, depressing emotions, and other trifling causes suffice to bring on dyspepsia accompanied by flatulence and diarrhœa. These cases may linger for years. Usually they improve during the summer in England, getting worse during the winter and spring, or during cold damp weather. Ultimately

Digitized by Google

the patients die from general atrophy, diarrhœa, or some intercurrent disease.

Morbid anatomy.—Post mortem, the tissues in sprue are abnormally dry; fat is almost completely absent; the muscles and the thoracic and abdominal viscera are anæmic and wasted. The liver is atrophied to half its normal weight, or even less; the spleen, adrenals, heart, and in fact all the viscera, are wasted approximately to the same degree. With these exceptions and certain important changes in the alimentary tract, so far as known, there are no special lesions which are invariably associated with this disease. According to Bertrand and Fontan, occasionally certain changes are present in the pancreas—namely, fatty or granular degeneration of the cells, with softening of isolated acini and slight inflammatory infiltration of the connective tissue. These, however, are not more constant than are certain other and similar changes occasionally found in the liver and kidneys. Sections of the tongue show desquamation of the epithelium, especially from the surface of the fungiform papillæ; the invasion of the epithelial cells by yeast fungi which has been shown by Kohlbrügge as well as by the Editor to take place is possibly a terminal infection.

Lesions of the alimentary tract.—The principal and characteristic lesions are found in the alimentary tract. The bowel is thinned to such an extent as to be almost diaphanous. The serous coat is generally healthy, the muscular coat atrophied. The submucosa in places has undergone hypertrophic fibrous changes; and the mucous membrane from mouth to anus, either in patches or universally, is superficially eroded and interstitially atrophied. The internal surface of the bowel is coated with a thick layer of grey, tenacious mucus containing numerous yeast cells and branching mycelium, which conceals patches of congestion, of erosion, or even of ulceration, besides such evidences of similar antecedent disease as pigmented areas and thin-scarred, cicatricial patches. The villi and glands are eroded, and in many places completely destroyed. Here and there minute spherical indurations, about the size of a pin's head and surrounded by a dark pigmented or congested areola, can be felt in the mucous membrane. On cutting into these, one finds them to be minute cyst-like dilatations of the follicles filled with a gummy, muco-purulent material. Sections of the diseased bowel show under the microscope corresponding changes, such as varying degrees of erosion or ulceration of the surface of the mucous membrane; degeneration of villi, glands,

Digitized by Google

and follicles; the small mucous cysts referred to; sometimes small abscesses; and, also, infiltration by leucocytes of the basement membrane and submucous layer; and, in the latter, fibro-cirrhotic changes (Fig. 100). The mesenteric glands are generally large and pigmented, perhaps fibrotic. The erosion lesions are usually most marked towards the end of the ileum and in the

Fig. 100.—Transverse section of ileum in case of sprue, showing partial loss of columnar epithelium (probably a post-mortem change), shrinkage of villi, round-cell infiltration, fibrosis of submucosa, and dilatation of nutrient vessels of submucosa. (*Orig.*)

colon; but they may be present in greater or lesser degree universally, or in patches throughout the entire alimentary tract from mouth to anus.

Pathology.—In attempting an explanation of the phenomena of sprue, two features of the disease have to be considered—the catarrhal condition of the alimentary canal, and the absence of the normal colouring matter of the fæces. Possibly one of these

Digitized by Google

is the consequence of the other; possibly the two conditions are concurrent but independent consequences of the same cause. What that cause may be is quite unknown. Whether the first pathological step originates in physiological exhaustion of the digestive functions, brought about by tropical conditions; or whether the disease depends upon a specific organism; or whether there is a combination of these, has still to be settled. In view of the occurrence of morning diarrhœa of dark bilious stools as a frequent first step in the development of sprue, hyperactivity of the liver might be assumed to be a first step in the development of the disease, an activity which in time ends in exhaustion of the chologenic functions of the gland. It might be further suggested that concurrently with this hepatic disturbance there is a similar initial hyperactivity of all the other glands appertaining to digestion, a hyperactivity which also ends in a corresponding exhaustion. Chemical changes in the ingested food would then follow on the establishment of these apeptic conditions, and ultimately, from the formation of acrid chemical bodies, lead to the chronic catarrhal changes found post mortem.

Analyses of the stools in sprue by Wynter Blyth, Hunter, v. der Scheer, Harley, and others resulted in ascertaining the presence of the ordinary elements of bile, notwithstanding their apparent absence so far as lack of colour would indicate. Bile is secreted, but the colouring matter, bilirubin, is not formed, or is changed in the intestine into a colourless substance, leucourobilin (Nencki). The excess of fat in the stools and the absence of pancreatic ferments would indicate pancreatic disease or destruction of the lacteal capillaries. The urine generally contains indican in the more acute stages of the disease; urobilin can also generally be demonstrated, and may be regarded as an indication of excessive blood destruction.

Of course, micro-organisms, and especially yeast fungi, abound in the fermenting stools; but hitherto no bacterium or protozoon which could be regarded as specific has been found in association with the disease.

One is inclined to regard sprue as the result of a specific infection falling upon structures subserving digestion, exhausted from over-stimulation by certain meteorological conditions. The remarkable effect of physiological rest, as supplied by "the milk treatment," in curing sprue, the relative rarity of the disease in the natives of the endemic area, the occasional latency of the disease, and the tendency to relapse seem to support this hypothesis.

Diagnosis.—The condition of the tongue, the character of

Digitized by Google

the stools, and the history are sufficiently distinctive, one would suppose, to render diagnosis an easy matter. Nevertheless, we have known of cases in which the disease has been diagnosed and treated as syphilis, the condition of the mouth being attributed to this disease, and the character of the stools and other symptoms being ignored. Care must be exercised in interpreting the significance of the small area of liver dullness usually found in well-marked cases of sprue. This is not due to cirrhosis of the liver, but to the wasting this organ undergoes in common with the rest of the soft tissues of the entire body. The absence of skin lesions and mental symptoms differentiates sprue from pellagra. No difficulty should be experienced in differentiating the sprue tongue from that of pellagra; in the latter disease it is pointed, and when it is inflamed and painful the process is found to be generalized over the whole organ and not localized to certain definite and circumscribed areas as in sprue. It is necessary to remember that atrophy of the lingual papillæ occurs in pernicious anæmia and even in malarial anæmia and ankylostomiasis, diseases all of which may from time to time be confused with sprue.

Prognosis is good for recent cases, provided proper treatment is carried out. It is bad for patients over 50, for long-standing cases, for careless and injudicious patients, and for those who cannot or will not take a purely milk diet.

Treatment. *Importance of early and thorough treatment.*—If treatment be undertaken sufficiently early, and be thoroughly and intelligently carried out, it is generally marvellously successful. Should, however, it be undertaken at too late a period, when the glands and the absorbing surface of the alimentary canal have been hopelessly destroyed, do what we will the case is sure to end fatally. In prescribing a treatment, therefore, the first thing for the physician to do is to get his patient thoroughly convinced of the deadly nature of his complaint; for, unless he receives the hearty and complete co-operation of his patient, he must not expect to cure a well-established case. To be successful, treatment must be thorough, sustained, and prolonged. All predisposing causes, as uterine or other discharges, syphilis, scurvy, and the like, must of course be dealt with and, so far as possible, removed.

The milk cure.—By far the most successful treatment is what is known as the "milk cure." In carrying this out it is well to commence with a dose of some aperient—castor oil or pulvis rhei compositus. Pending the action of the drug, all food, including

Digitized by Google

milk, should be withheld. The patient should be sent to bed in order to economize strength and maintain an equable warm temperature of the skin. He should also be directed to clothe warmly, to encircle the abdomen with a broad flannel binder, to cover his arms and shoulders with a warm jacket, and to live in a large, sunny, warm room. When the purgative has acted the milk is begun. At first 60 oz. at most are allowed in the twenty-four hours, small quantities being given every hour or every two hours. When the patient is very weak the feeding must be continued during the night. *The milk should not be drunk, but sipped with a teaspoon, or taken through a straw or fine glass tube, or from a child's feeding-bottle.* As a rule, on this regimen, in the course of two or three days, the patient's condition is very much improved. The stools have increased in consistency—are solid, perhaps, the distension of the abdomen has subsided, dyspeptic symptoms have vanished, and the mouth is much less tender and less inflamed. The quantity of milk should now be increased at the rate of half a pint a day or every second day, until 100 oz., or thereabouts, are taken in the twenty-four hours. It is well to keep at this quantity for ten days at least, when, everything going well, a gradual increase to 6 or 7 pints may be sanctioned. Up to this point the patient should keep in bed; but when he has reached this quantity he may get up and, if he feels strong enough and the weather is mild, go out of doors. *For six weeks, dating from the time the stools become solid and the mouth free from irritation, no other food or drink whatever should be permitted.* A raw egg, if it is found to agree, may now be added to the milk; later, some artificial malted food; next, small quantities of well-boiled arrow-root, rusks, pulled bread, thin bread (stale) and butter, or other digestible form of starchy food; later still, chicken broth, and a little fruit; and, by and by, fish and chicken may be gradually introduced.

Importance of prompt treatment of threatened relapses.—Should, however, the slightest sign of dyspepsia or flatulence, especially of diarrhœa, or of sore mouth, show itself, then the extra food must be discontinued immediately, a dose of compound rhubarb powder or castor oil administered, and the patient be sent back to bed and placed once more at absolute rest and on a strict milk diet. In convalescents, no matter how long the acute symptoms have been in abeyance, this prompt recognition and treatment of threatened relapse should be rigorously observed. This is a rule of the utmost value and importance. Procrastination in treatment, under these conditions, is exceedingly dangerous. Promptitude

Digitized by Google

in recognizing and treating relapse not only saves time, but may avert hopeless intestinal atrophy.

Symptoms persisting.—In commencing this treatment, if the patient after two or three days be found unable to digest and assimilate so much as 3 pints of milk in the twenty-four hours, the daily allowance must be reduced by half a pint a day until 30 oz. or thereabouts only are taken. If now the motions become solid, the quantity of milk must be gradually increased by 5 or 10 oz. a day, so that in the course of a few weeks the full allowance—6 or 7 pints—is consumed. In cases with persistent dyspepsia we have found pancreatic preparations of benefit. They may be given in the form of taka-diastase or Savory & Moore's pancreatic emulsion.

How to meet inadequate assimilation.—It sometimes happens that the quantity of milk can be raised to 70 or 80 oz. per diem but no higher, further increase bringing on sore mouth, distension, and diarrhœa. In some of these cases the difficulty appears to depend not so much on digestion as on inability to absorb a large quantity of fluid. Occasionally, in such cases, one may succeed in getting the necessary amount of nutriment introduced by thickening the milk with condensed milk; or by slowly evaporating fresh cow's milk so as to reduce its bulk without diminishing the solids (Thin). The evaporation is best done in a vessel like a glue-pot, in which the milk is not boiled, but is surrounded by a jacket of boiling water; the milk during the process must be constantly stirred to prevent the formation of a scum. Or the milk diet may be supplemented by an adequate allowance of raw or underdone meat.

Other forms of giving milk.—Digestion is sometimes aided by peptonizing the milk; or by mixing it with lime-water or a little salt; or by aerating it in a soda-water siphon. Koumiss sometimes agrees for a time when ordinary milk fails, and, if necessary, should be tried. Similarly, white wine whey is occasionally digested when milk is not; it is often of great service, especially when an alcoholic stimulant is indicated.

Fruit treatment.—The value of fruit in the treatment of sprue and other forms of intestinal disease has long been recognized by a limited number of practitioners, particularly abroad. It is only lately that it has obtained any hold on medical opinion in England. Manson had long been in the habit of prescribing bananas and apples, tentatively of course, in these cases, and often with marked success. Of late repeated trials of the strawberry in sprue have confirmed one's personal belief in the value of this fruit

Digitized by Google

treatment, and in the strawberry treatment in particular. The plan Manson followed was to give one or two strawberries with each feed of milk, and, if found to agree, to increase the number gradually until 2 to 3 lb. were taken daily. Preserved fruits, particularly peaches and pears, make suitable substitutes if strawberries or bananas are not obtainable. The bael fruit or Bengal quince (*Ægle marmelos*), introduced by Fayrer in the treatment of this disease, seems to exert a very beneficial effect in the countries (Ceylon and India) where it can be procured in a fresh state. Of recent years it has been imported from the East on ice, and offered for sale in London. Extracts, such as those sold in this country, appear to be inert. The ripe pulp should be scraped out of the hard exterior shell, and eaten raw with sugar and cream. Two or three fruits, depending on their size, may be given every day.

Treatment with meat juice and underdone meat.—Occasionally symptoms persist or become aggravated under the system of treatment described, and one is forced to conclude that milk does not suit the patient. In such cases raw-meat juice will often prove an efficient substitute. The juice of 4 or 5 lb. of fresh lean meat, and a little water to allay thirst, may be taken in small quantities at short intervals daily. After a time, when the stools are reduced in number and amount, although perhaps not quite solid, scraped meat, or very much underdone meat, and by and by a little charred toast, a plain rusk or biscuit, and so forth, may be gradually added to the diet.

Meat and warm water diet.—Not infrequently, after the stools have become solid under a carefully regulated strict milk diet, it is found that any attempt to return to ordinary food, or to take anything beyond the most simple farinaceous dishes, is quickly followed by a recurrence of diarrhœa and the familiar flatulent dyspepsia. Such cases are sometimes successfully treated by a complete abandonment of milk, fruit, and farinaceous stuffs for a time, and placing the patient on what is known as the "Salisbury cure." This is a diet consisting only of meat and warm water. Commencing with smaller quantities, in time the allowance of meat is gradually raised to about 3 lb. per diem, taken at equidistant intervals in three or four meals. The meat must be of good quality, free from fat, coarse fibre, and gristle; it may be prepared as mince, or in the form of steak or chop, not too much cooked. Warm water, amounting in all to 4 pints in the twenty-four hours, is drunk before going to bed and on rising in the morning, and also about two hours before meals—never at meals. This

Digitized by Google

course must be persisted in for six weeks, when ordinary food will be gradually attempted again. We have sometimes found it useful in cases of relapsing sprue to make the patient fast systematically one day a week, feeding him on that day on milk only. Sometimes, in cases of active sprue, we have found benefit from intermitting the strict milk diet for a day or two every week, and on these days feeding the patient on minced meat and hot water only.

Nutrient enemata or suppositories.—In all grave cases of sprue, nutrient enemata or suppositories should be steadily administered every four or six hours. If tolerated they are most valuable aids to nutrition. It is well, when using them, to wash out the rectum once a day with cold water.

These methods of treatment—followed by a carefully selected and increasing mixed diet, combined with warmth and rest—are, in our experience, the most successful methods of treating sprue; should they fail, the chances of recovery are poor indeed. Nevertheless, we have seen cases in which, after failure of the most carefully carried out milk or meat diets, a mixed diet proved successful for a time. In such mixed diets, in fact in all diets in sprue, *restriction in the amount* is as important, perhaps, as the quality of the food consumed. Food should never be given unless the patient is hungry. It is a great mistake to try to make these patients fat rapidly, or to stimulate the desire for food by encouraging active exercise. The bowel is not in a condition to deal with large meals.

When to send the patient to Europe.—When sprue develops in the tropics, if feasible the patient should be sent to Europe as soon as possible. It is a mistake, however, to ship an invalid with his disease active on him, or if his end is manifestly not very far off. Diarrhœa should not be active when the patient is put on board ship. In every case provision, such as a cow or an abundant supply of sterilized milk, should be made for carrying on treatment during the voyage.

The clothing and general management.—Sprue patients returning to Europe ought to be especially careful in their clothing, and they ought to get out their warm clothes before the ship leaves the tropics. If their return is during the winter, they should arrange to remain in the south of Europe till at least late spring. Next to an unsuitable dietary, perhaps cold is the most prejudicial influence to which a sprue case can be exposed. A sprue patient ought never to feel cold; he ought always to wear thick flannels, thick stockings, and, when up and about, thick boots. In winter

Digitized by Google

a chamois-leather waistcoat, provided with sleeves, is of great service. His rooms ought to be warm. He ought to eat very sparingly. He ought never to be fatigued; he ought to go to bed early and rise late; in fact, he ought to do everything in his power to avoid irritating the bowel, to guard against chill, physiological depression, and the necessity for copious eating.

During the summer England is suitable enough as a residence; but during the cold winter and spring months some milder, drier, and more sunny climate must be sought out.

Vaccine treatment.—Rogers in Calcutta and Nicholls in Colombo have recently reported apparently successful results by injection of vaccines made from the mouth—*Streptococcus viridans* or *S. salivarius*. Cultures are made from tongue scrapings or from aphthæ, and injected every five days, commencing with 50 millions and increasing gradually to 200 millions once a week. Should there be any reaction, dosage should be decreased. Michel, Martinez, and their collaborators in Porto Rico maintain that cures are obtained by injection of an autolysate of *Parasaccharomyces ashfordi*.

Drugs.—Experience soon teaches one to distrust medicines in sprue. Occasionally a gentle aperient or, if diarrhœa is watery and excessive, a few drops of laudanum are of service; but active drugging of all sorts is, as a rule, in the highest degree prejudicial. If the mouth is very painful, cocaine—5 gr. to the ounce—brushed on before eating will deaden sensibility and, for a time at all events, relieve suffering. Constipation must be carefully avoided, and a simple enema used if necessary.

It is right to state that two methods of drug treatment seem, in some cases, to have been followed by good results. One, advocated by Begg, consists in the administration of repeated doses of yellow santonin—that is to say, santonin which by prolonged exposure to bright sunlight has become yellow, or even brown. Begg insists on this change of colour, believing that it indicates a chemical change on which therapeutic value depends. The ordinary santonin obtained from the druggist he has found to be of no value in the treatment of sprue. Begg recommends one or two doses of castor oil to commence with, and thereafter 5 gr. of santonin in a teaspoonful of olive oil once or twice a day for a week, diet being at the same time attended to. The other method has gained for an irregular practitioner in Shanghai some reputation. It consists in the repeated administration of purgatives alternately with or before the exhibition of large quantities—two teaspoonfuls at a time—of some form of carbonate of lime,

Digitized by Google

believed to be powdered cuttlefish bone or powdered crab's eyes. Manson tried the santonin treatment without benefit to patients. He also used cuttlefish bone; in one case with the result of permanently stopping the diarrhœa but not of arresting the progress of the disease. In this case, although diarrhœa was most effectively checked, yet massive solid stools continued to pass. After a few weeks the patient died from asthenia, notwithstanding a liberal diet, which apparently was digested but not absorbed.

For the anæmia one may use intramuscular injections of small doses (10 min.) of arseniate of iron. In some instances the benefit from these injections has been prompt and marked. Their employment in every case of sprue in which anæmia is pronounced is recommended.

Flatulence and diarrhœa are sometimes relieved by massive doses of sodium bicarbonate.

The sprue patient, if possible, ought not to return to the tropics. If compelled by circumstances to do so, he must exercise the utmost care with regard to his health, and avoid exposure, cold baths, alcohol, and all excesses; take a minimum of, or avoid altogether, red meat; purge gently, and go on absolute milk diet on the slightest sign of relapse.

Digitized by Google

CHAPTER XXXII

HILL DIARRHŒA

Definition.—A form of morning diarrhœa accompanied by flatulent dyspepsia and the passage of copious liquid, pale, frothy stools. It occurs principally in Europeans on their visiting the hills after residing for some time in the hot lowlands of tropical countries.

Geographical and seasonal distribution.—Crombie, who gave an excellent account of this disease, pointed out that a similar affection may show itself in the highlands of Europe as well as in those of India. It is said also to occur in corresponding circumstances in South Africa and South America. There is no reason, therefore, to suppose that hill diarrhœa is special to India, although, owing to the large European population frequenting the hill sanitaria in that country, it has been particularly noticed there. An elevation of 6,000 feet or over, when combined with an atmosphere saturated with watery vapour, is particularly favourable to its development. In India it is found to begin and end with the rains, during which, in certain years and places, it is apt to assume almost epidemic characters. Thus, during the wet season of 1880, in Simla, an epidemic of hill diarrhœa affected from 50 to 75 per cent. of the population, three-fourths of the cases happening within a week of each other. In some years hill diarrhœa is less prevalent than in others; but at the proper season few of the various hill sanatoria of India are without examples.

Etiology and pathology.—It is difficult to say what may be the precise factors determining this disease. The low barometric pressure associated with great elevation above the sea-level may be a favouring circumstance. Damp seems to be indicated by the fact that the disease occurs principally during the rains. Chill after exposure to the high temperature of the plains has possibly an important share. Manifestly there is a suspension of the functions of the liver, and, considering the dyspepsia and looseness, most probably of those of the pancreas and of the other glandular structures subserving digestion. Hill diarrhœa is certainly something more than an intestinal catarrh. As Crombie pointed out, it is more in the nature of dyspepsia. There are no adequate grounds for connecting it with either the water or the food supply,

Digitized by Google

though at one time Duncan advanced the hypothesis that mica in the drinking-water caused irritation of the intestinal mucosa.

Symptoms.—Without very obvious cause the patient, who in other respects may be in good health, soon after arrival at a hill sanatorium becomes subject to a daily recurring diarrhœa, the looseness coming on regularly every morning some time between 3 and 5 o'clock. The calls to stool are apt to be sudden and imperative. The motions passed are remarkably copious; very watery in some instances, pasty in others. They are pale, frothy, and like recently stirred whitewash, so devoid are they of biliary colouring matter. Their passage is attended with little or no pain, often with a sense of relief. From one to half a dozen, or more, such stools may be voided before 11 A.M. After that hour, at all events in ordinary cases, the diarrhœa is in abeyance for the rest of the day, and the patient may then go about his duties or pleasures without fear of inconvenience.

The distinctive features of this form of diarrhœa are, therefore, the regularity of its recurrence every morning and its cessation after a certain hour in the forenoon; the absence of colour in the stools; and the attendant flatulence. The abdomen is sometimes blown out like a drum, the patient being conscious of unpleasant borborygmi associated with a feeling as if some boiling or chemical operation were proceeding in his inside. Occasionally cases are met with in which the stools are very pale although there is no diarrhœa.

Under treatment, or spontaneously, or, according to Crombie, on acclimatization occurring, after some days or weeks the diarrhœa may subside. In other instances it persists, in defiance of treatment, until the return of the patient to the warm plains, when it at once spontaneously subsides. Crombie instanced a case in which the patient was regularly attacked with hill diarrhœa whenever he visited Simla—twelve occasions—recovery invariably taking place on his return to the plains. If the looseness is both considerable and protracted, there necessarily ensue debility, wasting, and anæmia, and the disease may lapse into confirmed sprue—an affection having, apparently, close affinities with hill diarrhœa.

Treatment.—The treatment recommended by Crombie, and endorsed by other medical men of experience in India, consists in a strict milk diet, rest, warm clothing, a teaspoonful of liquor hydrargyri perchloridi in water about fifteen minutes after food, and 12 gr. of pepsin, or a corresponding quantity of lactopeptin or ingluvin, two hours later. If, in spite of treatment, the disease persists, the patient must return to the low country.

Digitized by Google

CHAPTER XXXIII

TROPICAL LIVER

THE subject of liver disease is everywhere a difficult and complicated one. It is especially difficult in tropical countries; for not only is the resident there liable to all the forms found in temperate climates, but he is exposed, in addition, to various potent predisposing and exciting causes of liver disease not present, or only present in a very mild degree, in more temperate latitudes. These additional causes of liver disease, inseparable from the tropics, are heat, malaria, and, especially, amœbic dysentery. To these, too often, have to be added injudicious personal habits, a tendency to over-full and over-rich feeding, to over-stimulation by alcohol, and deficiency of muscular exercise.

The young European who finds himself in the tropics for the first time is surrounded very often by luxuries in the shape of food, wine, carriages, servants—luxuries to which he had not been accustomed, perhaps, in his home. At first the change, the excitement of novelty, and the high temperature act as stimulants to appetite, and the excessive loss of fluid by cutaneous transpiration creates a powerful thirst. Little wonder, therefore, that in such circumstances the youth, having the appetite and the opportunity of gratifying it, is apt to indulge in food and drink beyond safe physiological limits. He is made lazy by the heat; he cannot exercise during the day, and when evening comes he prefers lounging on the veranda or hanging about the club bar to walking or riding or games. Very likely he sits up late at night, drinking and smoking, so that in the morning he is too sleepy to ride out or take any other form of exercise. And so it comes about, what with a surcharge of aliment and alcohol, and the diminished activity of lung metabolism and excretion incident to high temperature and muscular inactivity, that a very large and unusual amount of physiological work is thrown on the liver. With this large amount of work there is a corresponding hyperæmia. This may be considered the first stage of tropical liver—hyperæmia from functional activity; up to this point it is a purely physiological condition.

Pushed a step farther, this physiological hyperæmia passes

Digitized by Google

into congestion with blood stasis, and a consequent diminution of functional activity. Hyperæmia of a physiological character will be evidenced by increase of functional activity, and there will be a copious flow of bile, sometimes causing diarrhœa of a bilious character, particularly morning diarrhœa. But when the limits of physiological hyperæmia are passed, and congestion of a pathological character sets in, the consequent arrest of function will be evidenced by pale stools, perhaps diarrhœa of a pale, watery, frothy, fermenting character—in the last case the diarrhœa doubtless depending, in part at least, on fermentative processes set up in the contents of an alimentary canal no longer kept relatively aseptic by an adequate supply of healthy bile. Other symptoms of this condition are headache; furred tongue; scanty, high-coloured, loaded urine; a feeling of weight or fullness, or even of pain, in the region of the liver, and, probably, extension of the percussion area and other physical signs of enlargement of that organ. One step farther, and such a condition may pass into actual hepatitis attended with fever, smart pain in the liver, tenderness on percussion, and still more marked increase of the hepatic area.

A functionally very active hyperæmic organ is prone to inflammation, even on slight cause. In the case of the hyperæmic liver a common cause of inflammation is chill, such as may arise from a cold bath, a wetting, or from lying uncovered during a warm night in a current of air. The experienced resident knows this very well, and is at great pains to guard against such an occurrence. He very likely wears what is known as a cholera belt; he sleeps, even on the warmest night, in flannel pyjamas, and with a thin blanket drawn over his abdomen; during the day he wears a woollen undervest and very likely serge or thin tweed clothes. He does not sit down in damp clothes, and he has a great respect for a shower of rain. Besides chill, there are other causes which may convert the hyperæmia into congestion or inflammation; a blow may operate in the same way, so may a surfeit of eating or drinking, so may exposure to the sun, so may an attack of malarial fever, and especially of dysentery.

Treatment.—Nature sometimes effects a cure in these cases of hepatic congestion by establishing a smart diarrhœa. In the treatment of such cases we cannot do better than to imitate Nature, and even supplement her efforts. A few doses of the sulphates, in the shape of some kind of bitter water or of Carlsbad salts, generally give prompt relief. But if the subject of such attacks does not profit by experience and mend his ways, very likely

Digitized by Google

his liver, in time, will become chronically hyperæmic and extremely liable to intercurrent attacks of congestion of a character more or less acute. The subjects of this type of "liver" ought to be most careful in their habits. They must not lie abed too long; they must not take cold baths; they must not take cold drinks, nor expose themselves to cold in any form; they must clothe warmly; and they must eschew alcohol in every shape. Animal food they must partake of but sparingly; and they should give the preference to fowl and fish over beef and mutton. Fruit and farinaceous food may be more freely partaken of, but overeating in every form must be avoided. Exercise should be taken at least twice a day; and, at least once in twenty-four hours, the exercise should be of such a character as to provoke perspiration. A gallop on horseback, a smart game of tennis or rackets, are excellent hepatic stimulants. Occasionally, once a week or not so often, particularly when a sense of fullness or aching in the right side seems to indicate that all is not right with the liver, a dose of Carlsbad salts or bitter water, preceded perhaps by a few grains of calomel, may avert more serious trouble.

When hyperæmia becomes chronic, when the patient is continually suffering with "liver," he should leave the tropics for a time. Nothing relieves these cases of chronic congestion so quickly or so effectively as a visit to Carlsbad or to Harrogate, and a thorough course of the waters there and of the dietetic restrictions imposed in the Carlsbad cure. This should be followed up by country life in England and the active pursuit of country sports; the usual precautions in the shape of warm clothing, avoidance of cold baths, chills, alcohol, and high living being scrupulously observed, and a weekly saline purge taken.

A serviceable imitation of the natural Carlsbad water may be made by dissolving 53 gr. of the powdered salt in a pint of boiling water.* This may be divided into three equal portions, which are to be sipped as hot as possible, at intervals of twenty minutes, on an empty stomach, the first thing in the morning. While taking the solution, gentle exercise, as moving about the room, should be indulged in. Breakfast must not be taken till an hour after the last dose. If the bowels are not gently acted on, an increased quantity of the salts should be taken. During the course, which should be persevered in for three weeks, the diet must be carefully regulated: butter, fat, nuts, fruit, pastry, preserves, tinned foods, cheese, salads, wines, spirits, and beer

* A good substitute for Carlsbad salts consists of sod. sulph. 2 parts, sod. bicarb. 1 part, sod. chloride 1 part.

Digitized by Google

are to be avoided; too much meat must not be taken—a small meat meal once a day must suffice. The quantity of food, too, should be restricted, and clothing, exercise, and bathing be carefully attended to.

During a severe attack of acute congestion, or severe hepatitis attended with fever and much local distress, the patient must be kept in bed and placed on a very low diet of thin broths, barley-water or rice-water, or milk and water. He should be purged freely and often with salines. A large hot poultice, two feet or more in length by one foot in breadth, should be laid over the region of the liver; such a poultice to be effective should pass from the centre of the back to well over the epigastrium. Dry cupping sometimes gives marked relief. Muriate of ammonia has a certain reputation in these cases; it should be prescribed in 20-gr. doses every six or eight hours. We have often used it, but cannot vouch for its virtues; it does no harm.

When such a hepatitis is associated with dysentery, should it resist these milder measures hypodermic injections of emetine, as in amœbic dysentery, or 30 to 60 gr. of ipecacuanha, often give marked relief, and should be repeated every twelve or twenty-four hours for two or three times. When the hepatitis is associated with malarial fever, full doses of quinine, in addition to the purging and the other measures already mentioned, are indicated.

Whether hepatitis, unless associated with dysentery, ever passes on to suppuration is a moot point. Some say that it may; others resolutely deny that there is such a thing as "tropical abscess" unassociated with dysentery.

Digitized by Google

CHAPTER XXXIV

INFANTILE BILIARY CIRRHOSIS

WITHIN the last four decades a peculiar disease of the liver has been noticed in children in Calcutta and, to a less extent, in other large towns of India. It is found to be more prevalent in Hindu than in Mohammedan children. Thus, in Calcutta, from 1891 to 1893 inclusive, infantile biliary cirrhosis—the name given to this disease—caused 1,748 deaths. Although the Hindu and Mohammedan populations of that city are about equal, yet as many as 1,616 of the deaths occurred in Hindus, whilst only 80 occurred among Mohammedans, the balance of the mortality being among the Eurasians and other races. The disease occurs principally in children under one year, rarely attacking those over three years. As a rule, it commences during dentition, or about the seventh or eighth month, running a fatal course in from three to eight months. In rare cases it may commence within a few days of birth. Instead of lasting several months, its progress may be much more rapid, and terminate in death in from two to three weeks. The disease has many features in common with acute yellow atrophy of the liver and the peculiar hypertrophic cirrhosis described by Hanot in France.

The cause of infantile biliary cirrhosis is quite unknown; possibly reinvestigation will show that a proportion of the cases are infantile kala-azar. Neither alcohol, syphilis, nor malaria has anything to do with it. The children of the well-to-do are relatively more frequently attacked than those of the poor. It has also been observed that it tends to run in families, child after child of the same parents succumbing within a year or two of birth. The disease is probably always fatal.

Symptoms.—Commencing insidiously, the characteristic initial enlargement of the liver may have made considerable progress before the disease is suspected. Nausea, occasional vomiting, sallowness, feverishness, constipation, anorexia, irritability of temper, thirst, and languor call attention to the child's condition. On examination the liver is found to be enormously enlarged, extending perhaps to the umbilicus or even lower. The surface of the organ is smooth; the edge, at first rounded and prominent,

Digitized by Google

as the liver begins to contract becomes sharp and distinct and can be readily grasped between the fingers, the swollen organ feeling hard and resistant. The spleen may be enlarged, as in most hepatic cirrhoses. Fever of a low type sets in; the sallowness deepens into profound jaundice; the stools are clay-coloured, the urine is dark with bile, and there may be a terminal ascites, with puffiness of the feet and hands. The skin may be bronzed almost as deeply as in Addison's disease. Sooner or later death from cholæmia ensues.

Morbid anatomy and pathology. — Gibbons, who has given an elaborate and most careful account of the pathological anatomy of this disease, concludes that it is a peculiar form of biliary cirrhosis, the consequence of the action on the liver cells of some irritant of gastric origin, which leads to degeneration of the cells in the first instance, with subsequent increase of intercellular connective tissue and, later, of the portal sheaths. The formation of new bile-ducts between the hepatic cells, which is a well-marked feature, he regards as evidence of a natural curative effort having for its object a regeneration of the liver cells.

Treatment.—Hitherto, in this disease, treatment has been of little avail. There is some ground, however, for thinking that early removal from the endemic locality, and a complete change of wet-nurse and food, might have a beneficial effect.

Digitized by Google

CHAPTER XXXV

EGYPTIAN SPLENOMEGALY

Synonyms. — Splenic Anæmia ; Pseudoleukæmia Infantum ; Simple Splenomegaly ; Banti's Disease.

Definition. — A common disease in Egypt, having many features like those characteristic of infantile kala-azar, and causing anæmia, febrile disturbances, cirrhosis of the liver, and ascites.

Endemiology and etiology.—This disease is chiefly known from the writings of Richards, Day, and Ferguson, based on material obtained in Egypt. Splenomegaly associated with cirrhosis of the liver is common in all parts of Upper and Lower Egypt, where 20 per cent. of infants under 4 years of age are found to have splenic enlargement and anæmia. It is found in an easily recognizable form in 10 per cent. of autopsies performed at the Kasr-el-Ainy Hospital in Cairo. It has many features in common with infantile kala-azar as known in Southern Italy and the disease called Banti's disease. It is common at all ages up to 30 ; in the young it is apt to run a severe course, while at a later age the chronic form, progressing to ascites, is met with. The poorer native classes are chiefly attacked ; no case has ever been seen in the well-to-do, or in a European. In children the disease is generally associated with rickets ; in adults, with schistosomiasis and ankylostomiasis.

Symptoms.—The symptoms appear to be more objective than subjective. There are irregular fever, wasting, and a striking pallor. The spleen is obviously enlarged, hard and firm, often reaching to the umbilicus ; the liver also is enlarged in the early stages. Vomiting and diarrhœa are frequent complications, and in the later stages œdemas of varying degree and purpuric rashes may ensue. The fever is generally irregular in type and intermittent, and not amenable to quinine. The splenic enlargement causes pain and discomfort, especially after meals, and a dragging sensation on exertion. The symptoms complained of by the patient are those mainly caused by debility and anæmia. With the further progress of the disease the pyrexia increases, with steady enlargement of the liver and spleen causing expan-

Digitized by Google

sion of the costal angle. Hæmatemesis often occurs, but jaundice is rare. The final stage is ushered in by cirrhotic changes in the liver, which becomes hard and firm, and shrinks within the costal margin. The spleen also becomes fibrotic, but does not decrease in size. Pain, due to perisplenitis and perihepatic adhesions, increases; vomiting is a common feature. At last, ascites of considerable magnitude, due to hepatic cirrhosis, sets in (Fig. 101), and the patient becomes very much emaciated. The abdominal

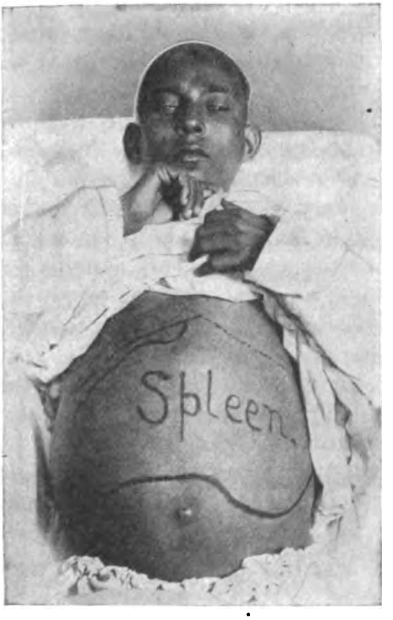


Fig. 101.—Egyptian splenomegaly. *(After Richards and Day; by permission of "Brit. Journ. Surg.")*

distension is now very great, and death supervenes, generally from pulmonary complications.

The blood picture varies at different stages of the disease. At the outset there is a distinct leucocytosis of 17,000, and myelocytes may be present. Afterwards a progressive anæmia of the chlorotic type becomes apparent, with a leucopenia of 3,000 and a mononuclear increase of 10–17 per cent.

Among the rare complications, thrombosis of the portal vein and hepatic carcinoma have been recorded.

The course of the disease is generally protracted; in older

Digitized by Google

children and adults it may run twenty years or more. Ascites is always an unfavourable symptom.

Morbid anatomy and pathology.—This has been accurately described by Ferguson. The average weight of the spleen is 30 oz.; it may reach 300 oz. It is firm in consistency; microscopically there is a general hyperplasia with active phagocytosis of the red cells by macrophages. The liver is generally enlarged in the early stages, and presents the picture of early multilobular cirrhosis with isolated necrotic foci. In the more advanced stages the organ is shrunken and firmly fixed to the diaphragm by adhesions. There is a comparative absence of bile-duct formation. The bone-marrow shows no great disturbance of the hæmopoietic system.

Diagnosis.—This must be made upon clinical grounds. No Leishman-Donovan bodies have as yet been demonstrated. Certain cases of *Schistosoma mansoni* infestations with hepatic cirrhosis and splenomegaly may closely resemble the condition, though no difficulty should be experienced in demonstrating the characteristic ova in the tissues. Visceral syphilis must be borne in mind.

Treatment.—No drug has so far been found to be of any avail. According to Richards, in cases with ascites, palliative operative interference, such as frequent tapping and the Talma-Morison operation (omentopexy), is permissible. In early cases, before the development of ascites, Owen Richards has performed splenectomy in 22 cases, with apparent success in 18. Whether the improvement in their general condition is maintained remains to be proved.

Digitized by Google

Section IV.—INFECTIVE GRANULOMATOUS DISEASES

CHAPTER XXXVI

LEPROSY (ELEPHANTIASIS GRÆCORUM)

Definition.—A chronic infective granulomatous disease produced by a specific bacterium, and characterized by lesions of the skin, nerves, and viscera, eventuating in local anæsthesia, ulceration, and a great variety of trophic lesions. After a long course it is almost invariably fatal.

History.—The many allusions in the oldest Chinese, Indian, Syrian, and Egyptian writings to a chronic, disfiguring, and fatal affection, possessing well-marked and characteristic skin lesions, warrant us in concluding that the disease now known as leprosy was as common and familiar in the East in times of remotest antiquity as it is at the present day.

Possibly leprosy is of comparatively recent introduction into Europe. The earlier Greek and Latin writers do not mention the disease. Most likely it was introduced from Egypt into Greece between 400 and 345 B.C. In the time of Celsus—53 B.C. to A.D. 7—it was still a rare disease in Italy; but during the early centuries of our era it increased there, and, probably following in the wake of the Roman conquests, it appears to have spread thence over the greater part, if not over the whole, of Europe. By the end of the seventh century it was well known in Spain, France, and Lombardy, and was first alluded to in England about the year 950.

So common was leprosy during the Middle Ages that the rulers and clergy of nearly all European states, becoming alarmed at its rapid extension and terrible ravages, took measures, by instituting leper asylums and enacting stringent laws for the segregation and isolation of lepers, to restrict the spread of what was speedily becoming almost a general calamity. By degrees the disease died out, the last indigenous British leper dying in Shetland in 1798. In Italy, France, Spain, Germany, and Russia the repressive measures were almost equally successful, although in these countries, in Greece, and in the Greek islands leprosy of

Digitized by Google

indigenous origin is still occasionally to be seen. It still lingers in Norway, where, in places, it is by no means uncommon (in 1890 there were 1,100, in 1906 under 500 known lepers); but even here, under a system of segregation and comparative isolation, it is rapidly disappearing. Apparently leprosy was introduced into the New World in the days of the slave trade.

We owe our modern knowledge of leprosy to Danielssen and Boeck (1848), to Virchow, Vandyke Carter, and others, while the discovery in 1874 by Hansen of the specific cause of leprosy —the *Bacillus leprœ*—has given a much-needed precision to our ideas on the important subjects of heredity and contagion, and on other practical points bearing upon the question of the leper as a source of public danger and upon his treatment and management.

Geographical distribution.—Whatever may have been the case formerly, at the present day, with unimportant exceptions. leprosy is a disease more particularly of tropical and subtropical countries. So generally is it diffused in these that it would be easier to specify the tropical countries in which leprosy has not, than to enumerate those in which it has been ascertained to exist. Moreover, it is probable that in many of the countries not yet positively known to harbour the disease it does really exist; for experience shows that the endemic area of leprosy enlarges as our knowledge of the natives of the uncivilized regions of the earth becomes more intimate. It may be safely concluded, therefore, that, with the exception of a few insignificant islands, leprosy is an element, and often an important element, in the pathology of nearly all warm countries.

The only tropical country of any magnitude about which we have anything like accurate leprosy statistics is India; and even in this instance the figures for many reasons are untrustworthy. According to the census of 1891, after making allowance for error, it is estimated that in British India there were 105,000 lepers in a population of 210,000,000—a ratio of about 5 in 10,000. Respecting China, of all countries probably the one in which there is the largest number of lepers, we have no figures to go by; but, judging from what is seen in the coast towns and treaty ports, the number of lepers is probably sensibly greater than in India. In Japan, in the Philippines, in Cochin China, in the Malay Peninsula, in the islands of the Eastern Archipelago and of the South Pacific, in Persia, Arabia, and Africa, the disease is common enough. The same may be said of the West Indies and of the tropical regions of America.

Digitized by Google

As regards more temperate countries, we know that there are considerable numbers of lepers at the Cape, a few in Australia, and a good many in Iceland.

Recent introduction.—An interesting and, from the etiological standpoint, an important circumstance about the geographical distribution of leprosy is its appearance and rapid spread in recent times in certain islands whose inhabitants, there is good reason to believe, had previously been exempt. This modern introduction of leprosy into virgin soil, so to speak, has taken place in the Sandwich Islands, in New Caledonia, and elsewhere. In the Sandwich Islands leprosy was noted among the aborigines for the first time in 1859, and soon spread so rapidly that by the year 1865 there were 230 known lepers in a population of 67,000. By 1891 the native population, from various causes, had diminished to 44,232; of these 1,500 were lepers—about 1 in 30. In New Caledonia leprosy was unknown until 1865. Its rapid diffusion throughout the island can be, and has been, traced step by step. In 1888 the lepers there numbered 4,000.

Etiology. *Age.*—It is open to question if leprosy has ever been seen in the fœtus. It has once or twice been reported in the newly born. Cases are also on record of its occurrence as early as the first and second years of life; such cases, however, are quite exceptional. Leprosy is extremely rare before the fifth or sixth year. In the great majority of instances the disease begins between the tenth and thirtieth year. It rarely commences after 40, although it has been known to begin up to and even after 70.

Sex; occupation; social and hygienic conditions.—Apart from social conditions as affording opportunity for contagion, sex seems to have little bearing on the liability to leprosy. The same may be said of occupation, and social and hygienic conditions in general. Very probably bad food and bad hygienic circumstances have in this, as in most germ diseases, a predisposing influence; but they certainly cannot create a lepra bacillus and leprosy, any more than they can create an acarus and itch. This is abundantly shown by the absence of leprosy at an earlier period in countries in which, without alteration in the food or other hygienic conditions, the susceptibility of the natives to the disease was subsequently proved by its rapid spread on being introduced from without, e.g. the Sandwich Islands and New Caledonia; and also by the disappearance of the disease, in other instances, under the influence of the segregation and isolation of lepers, without any concurrent material alteration in food or other circumstances, e.g. Scotland, Ireland, and most European countries.

Digitized by Google

Sir Jonathan Hutchinson very sagaciously and truly remarked that leprosy is more especially a disease of semi-civilization. Savages are exempt; the highly civilized are exempt; but when the savage begins to wear clothes and live in houses he becomes subject to the disease. In other words, in the early stages of civilization opportunities of infection are multiplied, and their influence is not counteracted by cleanliness of house or person.

Climate.—Climate can in no way be considered a cause of leprosy, for leprosy exists in all climates and in all latitudes. But it does seem to have some influence in determining, to a certain extent, the type the disease assumes. It would appear that the nodular form is more common in cold damp climates; the nerve form, in warm or dry climates.

Conveyance of the lepra bacillus from man to man.—Many attempts have been made to communicate leprosy to man by inoculation; hitherto, with one questionable exception, all have failed. A Sandwich Islander, apparently at the time free from leprosy, was inoculated from a lepra nodule. Within a month he had symptoms of leprous neuritis; two years later he was a confirmed leper; and in six years from the date of the inoculation he died of leprosy. Unfortunately the subject of the experiment was a native of a country in which leprosy was extensively endemic, and, besides, he had lived among lepers; in fact, members of his family were lepers.

To bridge over this important gap in the evidence, we have to fall back on the close analogy that subsists between *Bacillus leprœ* and *B. tuberculosis*, the leproma and the tubercle, leprosy and tuberculosis. In consideration of this and other circumstances, it is generally conceded that *B. leprœ* is the cause of leprosy, just as *B. tuberculosis* is the cause of tubercle. Authorities differ, however, as to the way in which the bacillus is acquired.

How acquired.—There are two principal views as to the way in which the bacillus is acquired—heredity and contagion.

Heredity. — From the fact that it tends to run in families and that in certain instances it assumes the appearance of atavism, leprosy, until the *Bacillus leprœ* was discovered, was almost universally—as it still is by some—believed to be an hereditary disease. Yet if leprosy be communicated generally, or even sometimes, by parent to child by heredity, how explain the striking fact, brought out by Hansen, that of the numerous offspring of 160 Norwegian lepers who emigrated to America not one has become a leper?—or, again, the equally well attested fact that children sometimes become lepers first, their parents afterwards?

Another powerful argument against the doctrine of heredity is the circumstance that lepers become sterile early in the disease. From this it is

Digitized by Google

evident that unless the ranks of leprosy are recruited in some other way than by heredity the disease would inevitably die out in one or, at most, two generations.

From considerations such as these the view that leprosy is an hereditary disease has now few adherents among the well informed.

Contagion.—With few exceptions, the best authorities believe that leprosy is propagated by contagion, and only by contagion. The same unanimity of opinion does not obtain as to the particular way in which, or medium by which, the contagium is applied; but that it passes, directly or indirectly, from the infecting leper to the recipient, nearly all are agreed to regard as being practically proved. The principal facts and considerations on which this important conclusion is founded are as follows:—

That the habitat of the infecting germ is man is rendered in the highest degree probable by the fact that the germ is found in the human tissues and, hitherto, nowhere else; and by the fact that leprosy has never been known to appear in virgin soil independently of the prior advent of a leper. When a leper settles down in virgin country, after a time cases of the disease crop up among his companions and immediate neighbours. Some of these newly-made lepers, proceeding to a different part of the country, in time become centres for other groups of cases. Thus, in the early history of the introduction of leprosy into a virgin country—as New Caledonia—the spread of the disease from individual to individual, and from place to place, can be, and has been, traced.

In further proof it can be advanced that not only may a native of a non-leper country acquire the disease on visiting a leper country, but he may also communicate the disease to others, his countrymen, on his return to his own country. There is at least one well-authenticated example of this on record. Dr. Hawtrey Benson, in 1872, showed at the Medical Society of Dublin a leper, an Irishman, who had acquired his disease in the West Indies. After his return to Ireland he slept in the same bed as his brother, who, moreover, sometimes wore the leper's clothes. In time this brother, who had never been out of the United Kingdom, became a leper, and was shown to the same medical society in 1877. In this case there can be no question of fact or of diagnosis—such a case can only be explained by contagion. Though not quite so well authenticated and conclusive, many similar instances of the communication of leprosy by contagion are on record. The case just mentioned is alone almost conclusive; for if leprosy is proved to be communicable by contagion in one case, the probabilities are that it is so acquired in every case.

It has been advanced against the contagiousness of leprosy, that it attacks a very small proportion only of the attendants, nurses, and doctors in leper asylums. But might not a similar objection be raised to the contagiousness of scabies or of ringworm? The conditions for successful contagion are known and can be easily avoided in the latter diseases; they are not known and are therefore not invariably avoided in leprosy. All contagious diseases demand certain conditions for their diffusion. In some diseases these conditions are easily complied with and often concur; in other diseases they are with difficulty complied with and rarely concur. Leprosy belongs to the latter category.

Probably intimate personal contact, and certain concurrences in the phases of the disease with special conditions in the health

Digitized by Google

or physiological state of the recipient, are necessary for the successful communication and acquisition of leprosy. The simple implantation of the bacillus does not suffice; for, as already pointed out, of the many inoculations that have been made only one has any claim to be regarded as having been successful.

Sir Jonathan's Hutchinson's theory that imperfectly cured fish is a medium of infection has not obtained general acceptance.

Bacillus leprœ.—The lesions of leprosy are the result, direct or indirect, of the proliferation of the *B. leprœ* in the tissues. This

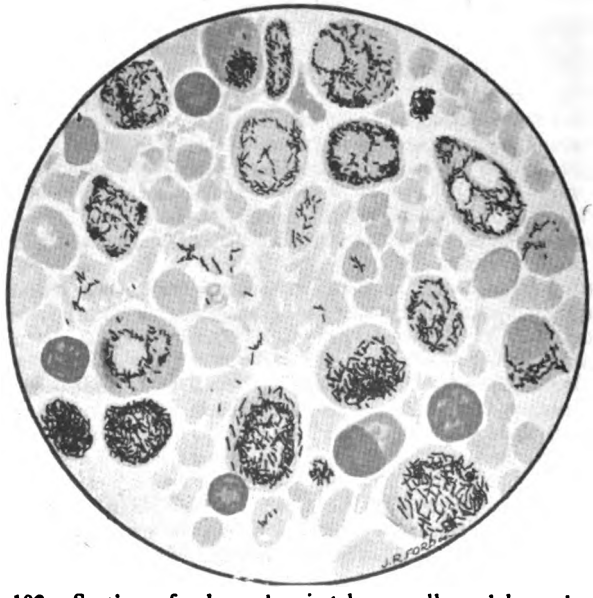


Fig. 102.—Section of spleen showing lepra cells and lepra bacilli. × 800. (*Orig.*)

parasite (Fig. 102) in size, shape, and staining reactions closely resembles the bacillus of tubercle. In length it is from half to two-thirds, and in breadth about one-sixteenth the diameter, of a blood-corpuscle. The ends of the rod—which is always straight—are in many specimens somewhat attenuated; and in many instances—presumably in old bacilli—a moniliform arrangement of the protoplasm, as if from spore-formation, or, according to Hansen, from disintegration, can be detected. By some authorities it is said to possess a gelatinous capsule. In common with *B. tuberculosis* and *B. smegmœ* it retains carbol-fuchsin stains after being treated with mineral acids.

Digitized by Google

It is stated that it may be distinguished from *B. tuberculosis* by its staining more readily with cold weak solution of carbol-fuchsin, and by being decolorized more easily with dilute acids; by the impossibility hitherto experienced of growing it on the usual culture media, and of successfully inoculating it into man and the lower animals; by its tendency to occur in dense clusters and in greater numbers; and by its very generally being found inside cells or, according to Unna, in zooglœa masses in the lymphatic spaces.

Specimens of the bacillus can be procured readily by excising a portion of a leproma—a proceeding, in consequence of the absence of sensation in most tubercles, not usually much objected to by lepers; or they may be obtained by including a succulent leproma in a pile clamp, slowly screwing up the jaws of the instrument so as to drive out the blood, pricking the now pallid leproma, and then collecting on a cover-glass the droplet of "leper juice" which exudes from the puncture. The juice may be spread out on the cover-glass, fixed, stained, and decolorized as for the demonstration of tubercle bacilli; or it may be examined fresh. Better preparations are obtained by making with a small scalpel a minute incision into the compressed leproma, scraping some of the tissues from the under surface of the skin, and smearing this with the juice on to the cover-glass. One must be careful to exclude the possibility of contamination with *B. tuberculosis*, with which lepers are often infected.

If examined fresh, or if a morsel of leproma be teased up in water, the bacilli may be seen both inside and outside the cells and in active motion. Whether this motion is simply molecular, or whether it is vital, is hard to say; probably the former, for, whilst osmic acid does not stop it, it is immediately arrested by the addition of a viscid fluid—for example, glycerin or albumen water.

The bacillus is found in all primary leprous deposits; in the skin leproma—where it occurs in prodigious numbers; in the meagre infiltration of the macular eruptions—where it is much more sparsely distributed; in the early stage of leprous neuritis—where, also, it is present only in small numbers; in the specific lesions of the liver, spleen, testes, lymphatic glands, and lungs—where the lesions may resemble those of tuberculosis or may be invisible to the naked eye. In the blood-vessels it has been found in the endothelium and, occasionally, free in the blood or enclosed in leucocytes. It is abundant in the purulent discharges from the nose, from ulcerating lepromata or other forms of primary

Digitized by Google

leprous infiltration. It has very rarely been found in the spinal cord or in the lungs. It is doubtful if it occurs in the brain, the intestinal tract, or in the kidneys, although the latter are prone to inflammation in leprosy. It is not found in muscle, in bone, or in cartilage; and it is not necessarily present in the secondary trophic lesions of nerve leprosy, or in secondary inflammatory effusions.

Many apparently unsuccessful attempts have been made to cultivate the lepra bacillus. The word "apparently" is used because some modern leprologists consider that probably a proportion of these attempts were successful, although at the time not regarded as being so. Mycotic forms developed in the culture media, but as these forms were not acid-fast they were regarded, at the time, as contaminations and not growths of the lepra bacillus. A modern view is to the effect that *B. leprœ* is really a streptothrix like the actinomyces, or, according to some, that like the tubercle bacillus it is pleomorphic to a high degree, and that at a certain stage of growth and under certain conditions the mycelia break up into short rods, many of which are now acid-fast. There is great discrepancy of opinion among bacteriologists on the subject, each observer having his special lepra germ grown on his special culture medium; this germ he regards as the only true one, conforming, he claims, to the proper agglutination and complement-fixation tests, and its products possessing a therapeutic value comparable to that of tuberculin, and giving rise to a local and a general reaction when injected into lepers. Other bacteriologists, though following the methods that have succeeded in the hands of their authors, have generally failed to obtain similar results. For instance, Fraser, using the special placental juice, horse-serum-nutrose-agar, was unable to confirm the results reported by Bayon, Duval, and others.

Rat leprosy.—The discovery that rats (5 per cent. in Paris) are subject to a disease clinically resembling human leprosy may lead to a better knowledge of the lepra bacillus, seeing that the lesions of the "rat leprosy," as it is called, are intimately associated with an acid-fast bacillus resembling that of human leprosy, and that it is communicable to other rats by association.

Pathological anatomy.—The young leproma presents a smooth, white, glistening section. When the leproma is older the cut surface has a brown tint, and the morbid tissue may become, from fibrotic changes, harder, or, from degeneration, softer. The specific lesion of leprosy differs from that of tubercle inasmuch as the former is well supplied with blood-vessels, contains no true giant cells, and never undergoes caseation. If hardened, cut, stained,

Digitized by Google

decolorized, and examined under the microscope, the leproma is found to consist principally of small round cells about the size of a leucocyte, epithelioid cells, and fusiform cells—the two latter in numbers increasing with the age of the leproma. It can be seen that these cells have infiltrated and partially dissociated all but the most superficial layer of the derma. It may be further observed that the cells are arranged for the most part in groups, generally around and near blood-vessels; and that a very large proportion of them contain bacilli, some cells having only a few, whilst others are literally crammed with the organisms. Isolated bacilli are also found scattered through the preparation, apparently free in the lymph spaces. The bacilli are never seen inside the nuclei of the implicated cells.

In addition to the bacilli-bearing cells, and increasing in number with the age of the lesion, a number of brown granular bodies, larger and smaller, which have been named "globi," are to be found. These Hansen holds to be cells in which the bacilli have perished and become granular. It is to them that the brown colour of old lepromata is due.

Other lesions.—The histology of the infiltrated macula is practically the same as that of the leproma, the number of bacilli, lepra cells, and globi being proportionately fewer. In old maculæ, as in very old lepromata, the bacilli may be hard to find or entirely absent. In the anæsthetic maculæ the terminal nerve fibres are degenerated.

As the fusiform thickening of the larger nerve trunks in nerve leprosy is a secondary inflammation, bacilli may not always be found in it, although, at the very commencement of the nerve disease, bacilli, both in cells and, according to Leloir, free between the axis cylinders, are present and may even lie in the nerve tubules themselves. In time the affected nerves become mere fibrous cords destitute of nerve tubules.

The anatomy and histology of the various trophic lesions are such as are found in other examples of destructive neuritis, and are in no way peculiar to leprosy; they do not, therefore, call for description here.

In nodular leprosy the liver and spleen are the seat, in many instances, of a peculiar infiltration which, in well-marked examples, may be visible to the naked eye. Fine yellowish-white dots and streaks are seen to occur in the acini of the former. These dots and streaks consist of new growth in which bacilli abound.

In all cases of nodular leprosy the testes atrophy and undergo fibrotic changes, bacilli and globi being found both in and around the tubules, free and in cells.

In all forms of leprosy the lymphatic glands appertaining to parts in which leprous deposit is present are characteristically affected. They are swollen and hard, and on section the gland tissue is seen to have a yellowish tinge from an infiltration which contains numerous bacilli and globi.

Albuminoid disease of the alimentary canal, liver, and spleen, and nephritis occur in a large proportion of the cases of nodular leprosy.

Diagnosis.—The touchstone in all doubtful cases is the presence or absence of anæsthesia in some skin lesion or in some skin area. Anæsthesia is rarely absent in leprosy; generally in the implicated spots it is complete, or nearly so. It should be particularly sought for towards the centre of maculæ, in the pale patches left after the fading of former maculæ, in the hands and feet, and in nodules

Digitized by Google

of some standing. In no other skin disease is definite anæsthesia a symptom.

Vitiligo or *leucodermia*—sometimes called white leprosy, and by the vulgar very generally regarded as true leprosy—bears a certain resemblance to the pale postmacular patches referred to; not to mention other features, the absence of anæsthesia in leucodermia at once settles diagnosis.

Further assistance may sometimes be got in doubtful cases from the fact that leprous spots rarely perspire. A hypodermic injection of pilocarpine is of use in bringing out this point.

The sensory and trophic lesions of *syringomyelia* might be mistaken for nerve leprosy, but the general history of the case, the history or presence in leprosy of macular eruption, of thickened nerve trunks, and of enlarged lymphatic glands, and their absence in syringomyelia, are mostly sufficient to establish a diagnosis.

The occurrence of an acid-fast bacillus in the sputum of a patient coming from a country in which leprosy is common should be regarded with suspicion, and its true nature tested by injection of the sputum into the guinea-pig.

It is hardly necessary to point out the diagnostic marks of leprosy as against syphilis,* erythema multiforme, erythema nodosum, trypanosomiasis, lupus vulgaris, lupus erythematosus, psoriasis, eczema, lichen planus, cheloid, body-ringworm, erythrasma, pityriasis versicolor, pellagra, elephantiasis arabum, etc. Mistakes can scarcely be made unless from carelessness, or by someone completely ignorant of the nature, history, and symptoms of these diseases.

In approaching the diagnosis of skin eruptions, localized pareses, muscular atrophies, and anæsthesia in patients living in or coming from a country in which leprosy is endemic, the possibility of their being attributable to this disease must be borne in mind. If doubt exist, and it be found feasible, search for the bacillus should be made in eruptions, or in thickened nerves, or in any nasal or other morbid discharge that may be present. If this be found the diagnosis of leprosy will be infallibly established.

Prognosis.—Complete recovery is an event so rare in leprosy that, though it may be hoped for, it must not be expected. Recovery from the actual disease itself—that is, in the sense that fresh leprous infiltration may cease to occur, and old infiltration may be absorbed, and that the bacilli may die out—is perhaps the rule in nerve leprosy; but the effects of the leprous process

* Unfortunately the Wassermann reaction is of little value, as the majority of leprous serums are said to give a positive result.

Digitized by Google

are generally permanent, the trophic lesions resulting from nerve destruction being irremediable. Such cases may live, however, for many years—thirty or forty—and die of some other disease.

Nodular leprosy is usually a much more acute disease than nerve leprosy, sapping the strength and general health much more effectually and more quickly. It rarely runs its full course, death being brought about by some intercurrent disease, such as, and especially, phthisis, nephritis, albuminoid degeneration of the alimentary tract, dysentery, stenosis of the larynx, or pneumonia. It may even prove fatal as a sort of "galloping" leprosy within a year of its first declaring itself.

Symptoms.—Although *B. leprœ* is the cause of all leprosy, the clinical manifestations of its presence are far from being identical in every case; indeed, they are almost as varied as are those of syphilis or of tubercle. As a matter of fact, in its earlier stages leprosy is far from being always, or even generally, a striking disease. Often for years the only visible evidence of its existence may be two or three small blotches, or perhaps one or two patches of pale or pigmented skin on trunk or limbs—very likely concealed by the clothes and perhaps disregarded by the patient himself—the true significance and nature of which can be appreciated only by the expert. It is generally not until the later stages that we see the disfiguring and extensive lesions on which the popular conception is founded. As a rule, it is a disease of very slow development. Sometimes, it is true, it is suddenly and frankly declared from the outset, and progresses rapidly; but in the vast majority of cases the early lesions are trifling and are apt to be misinterpreted and overlooked, and years elapse before serious mutilation or deformity is produced.

To facilitate description, it seems advisable to divide the evolution of leprosy into stages, premising, however, that the division proposed is in great measure an artificial one. What are here designated stages are not, all of them, clinically and in every instance, abruptly separated or even present; for the most part they merge imperceptibly into each other, and in not a few instances some of them cannot be recognized.

1. Primary infection.
2. Period of incubation.
3. Prodromata.
4. Primary exanthem or macular stage.
5. Period of specific deposit.
6. Sequelæ—ulceration, paresis, trophic lesions.
7. Terminations.

Digitized by Google

1. *Primary infection.*—Seeing that leprosy is caused by a specific germ, there must have been a time, in the history of every leper, when the infecting germ entered the body, but there is no local lesion to mark the spot. We are equally ignorant as to the condition of the infecting germ, whether it enters the body as spore or as bacillus, and also as to the medium in or by which it is conveyed. We cannot say whether it enters in food, in water, in air; whether it passes in through the unbroken epithelium, or whether it is inoculated on some accidental breach of surface, or, perhaps, introduced by some insect bite.

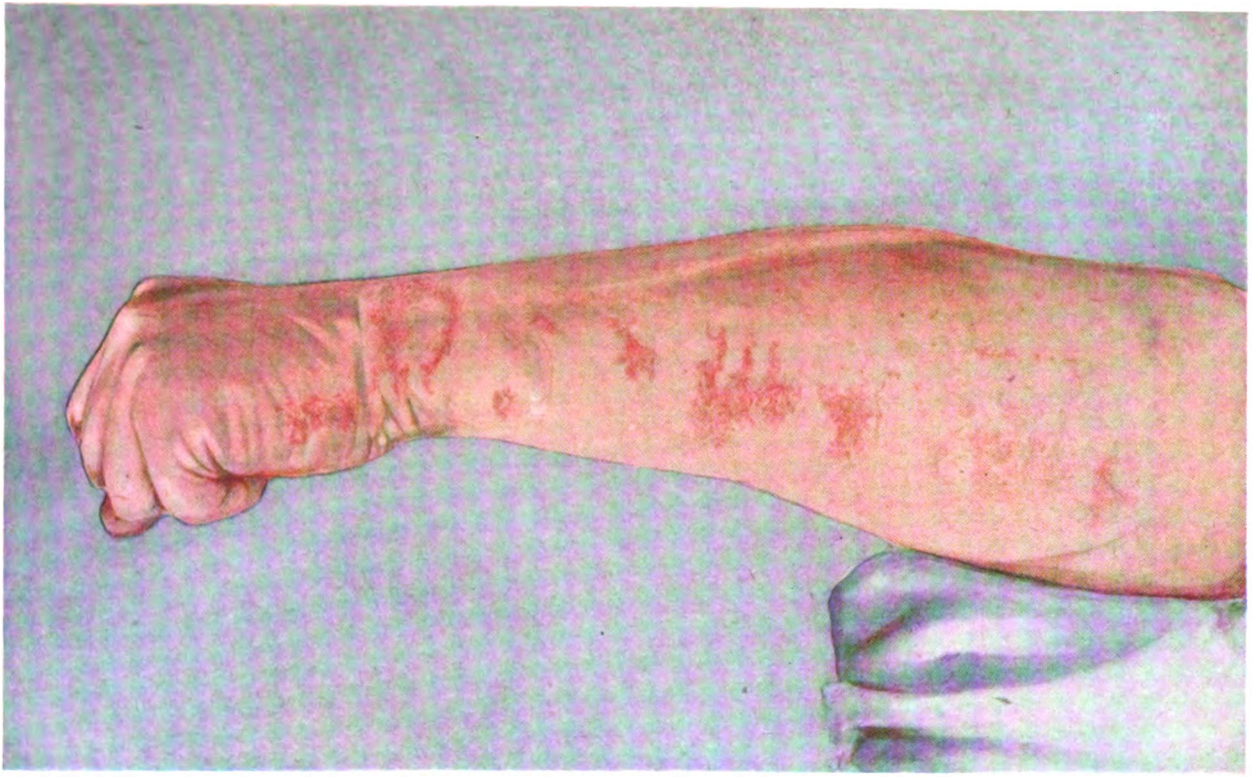
B. leprœ is found in the nasal mucus in the majority of early cases of leprosy. It is therefore considered that the initial lesion of the disease is a specific ulceration of the cartilaginous septum of the nose; this lesion persisting is an active source for the diffusion of infection, and may give rise to epistaxis.

Although we are in absolute ignorance as to the process of infection, we may be quite sure that in leprosy there is an act of infection, and that the infective material comes from another leper.

2. *The period of incubation.*—This is generally, possibly always, long, and has to be reckoned usually in years—two or three at least, it may be ten. Leloir and Höegh have described extreme cases in which the period varied between fourteen and twenty-seven years. On the other hand, cases are on record in which the incubation period was set down at three months or even at a few weeks.

3. *Prodromata.*—Fever of greater or less intensity and occurring more or less frequently is, almost invariably, a feature of the prodromal stage of leprosy. Febrile attacks with weakness and drowsiness may recur off and on during one or two years. It is well to bear in mind that in tropical countries such attacks are apt to be looked on as malarial. Dyspeptic troubles, associated with diarrhœa in some cases, with constipation in others, and usually attributed to "liver," are also common. Epistaxis and dryness of the nostrils, perhaps symptomatic of the initial lesion, perhaps corresponding to the epistaxis in the prodromal stage of typhoid and tuberculosis, have been noted. Headache; vertigo; perversions of sensations—such as localized pruritus, hyperæsthesia, "pins and needles," neuralgic pains—intermittent for the most part, and perhaps very severe, and especially common in the limbs and face; general aching, rheumatic-like pains in loins, back, and elsewhere; all or any of these, for months, may herald the explosion of unequivocal leprosy.

Digitized by Google



EARLY MACULAR RASH OF LEPROSY.

(By permission of London School of Trop. Med.)

Note distribution along the course of the ulnar nerve.

PLATE XX.

Digitized by Google

Digitized by Google

The liability in many instances to excessive sweating, which comes on without apparent or on very slight provocation, is another curious feature of early leprosy. As pointed out by Leloir, this hyperidrosis may be general or it may be confined to particular parts, most often the trunk, the limbs being unaffected or even being the subject of anidrosis. A still more limited anidrosis is sometimes found; it usually happens that these non-sweating spots become anæsthetic at a later period of the disease.

It should be noted that all prodromal symptoms may occasionally be absent.

4. *The primary exanthem.*—In a considerable proportion of cases, after a longer or shorter period of indifferent health, sometimes preluded by an outburst, more severe than usual, of fever and other prodromal phenomena, an eruption appears on the skin. (Plate XX.) This generally coincides with, or is soon followed by, an improvement in the general health.

Although strictly macular, this eruption—the primary exanthem of leprosy—varies, in different cases, in the size of the spots as well as in their number, duration, and other characteristics. They may be no larger than a millet-seed, or they may occupy surfaces many inches in diameter; they may be numerous, or there may be only two or three. The earlier spots are usually purely erythematous, disappearing on pressure, and being darkest in the centre and shading off towards the periphery. But in some cases they may be pigmented from the outset; or they may be mere vitiliginous patches; or all three forms of maculæ may occur in the same individual—erythematous, pigmented, and vitiliginous. In not a few lepers what in the first instance was an erythematous patch may in time become pigmented, or it may become pale; in the latter case the loss of pigment is usually associated with a certain degree of atrophy of the cutis. Or it may be that the centre of an erythematous patch clears up, the periphery of the patch remaining red and perhaps becoming pigmented; so that the affected spot comes to present the appearance of a red or dark ring, or portion of a ring, enclosing a patch of pale, usually anæsthetic skin. In certain instances the eruption of the various forms of maculæ may be preceded by local paræsthesiæ, such as a sense of burning, tingling, pricking, and so forth.

At first the maculæ may be evanescent and may fade wholly or in part in the course of a few days, weeks, or months; but as the disease progresses, and fresh spots appear, they tend to greater permanency, to be more liable to pigmentation, and are partially or wholly anæsthetic from the outset, or subsequently become so.

Digitized by Google

A striking feature of this and of all leprous eruptions is the loss of the hair in the affected areas. Another striking circumstance is the fact that the most hairy part of the body, the scalp, is never or very rarely affected either with leprous eruptions or with leprous alopecia. As the face, particularly the superciliary region, is prone to all forms of leprous eruption, depilation of the eyebrows is a very usual, very early, and very characteristic phenomenon. The beard, too, is apt to be patchy, particularly in nodular leprosy. In many instances, before they drop out, the individual hairs become white, or downy, or splintered, or monillated.

The most frequent seats of the primary macular eruption are the face, especially the superciliary region, the nose, cheeks, and ears; the extensor surfaces of the limbs; the backs of the hands; the back, buttocks, abdomen, and chest. The palms of the hands and the soles of the feet are rarely if ever attacked. At this stage of the disease the mucous membranes are very rarely affected.

In the distribution of the maculæ a rough symmetry may or may not be discernible.

5. *The period of specific deposit.*—During the stage just described, if there be any thickening of the skin or other evidence of new growth it is barely perceptible to sight and but slightly so to touch. Sooner or later, however, another stage is entered on, a stage characterized by the deposit or, rather, growth of a tissue possessing well-marked specific characters. This deposit occurs either in the skin, or in the continuity of the peripheral nerve-trunks, or in both. If in the first situation, nodular or, as it is sometimes called, tubercular leprosy is the result; if in the second, we have nerve or anæsthetic leprosy; if in both of these situations, then what is known as "mixed leprosy" is produced. These three forms of the completely developed disease, though having much in common, are, as a rule, clinically fairly distinguishable. It is customary, therefore, to describe them separately.

Nodular Leprosy.—This form of leprosy often appears without a well-marked preliminary macular stage, being ushered in, after a longer or shorter prodromal stage, by a smart attack of fever and the rapid development on the face or elsewhere of the specific lesion. In other instances a well-defined but, in comparison with nerve leprosy, short macular stage precedes the appearance of the characteristic lepromata.

The essential element in nodular leprosy is the leproma. The dimensions, the combinations, the situations, the growth, and the decay of this give rise to the more manifest symptoms of the earlier stages, at all events, of the disease. The leproma, which

Digitized by Google

has been more fully described in the section on the pathological anatomy of leprosy, is formed by infiltration of the deeper layers of the derma with what at first is a small-celled, somewhat dense neoplasm. As this slowly or more rapidly increases it forms a prominent, rounded boss or protuberance covered with unbroken epidermis. In size it ranges from the dimensions of a split pea, or of a bean, to a great plaque many inches across. In colour it differs according to its age and condition, and according to the natural hue of the skin of the leper; it varies from red to dirty pink in the earlier and congestive active stage, to dark brown or

TERZI.—

Fig. 103.—Nodular leprosy. (*After Leloir.*)

dirty yellow in the later stages. It is generally—though not always, especially at first—anæsthetic to some degree, if not absolutely so; it is devoid of hair, usually somewhat greasy-looking and, perhaps, stippled with gaping sebaceous follicles. Though not so hard as cheloid growth, it is fairly firm to the touch, and, unless very extensive, can be readily raised up and freely moved over subjacent structures. Isolated lepromata are usually round or oval; when contiguous they may coalesce, forming patches of irregular outline.

When many lepromata run together, or are closely set, the growth causes the natural folds of the skin to be exaggerated;

Digitized by Google

great disfigurement, especially of the face, may ensue (Fig. 103). The appearance becomes repulsive and "leonine."

Nodules may appear in greater or less profusion on the limbs and body; favourite sites being the backs of the hands, the external surfaces of the arms, wrists, thighs, and the groins. On the trunk they may occupy very large areas, forming extensive plaques. As a rule, in the latter situation they are not so prominent as on the face and arms. The same remark applies to the legs, where the infiltration is usually dusky, diffuse, ill defined, and prone to ulcerate.

From time to time, and at longer or shorter intervals, fresh lepromata appear, their formation generally concurring with an outburst of fever. The normal and usual fate of the nodule is either first to soften in the centre and then to be absorbed, leaving a smooth circular patch of scar tissue; or, after softening, to ulcerate and discharge a sticky, yellowish pus. This discharge tends to dry up into crusts, ulceration proceeding underneath.

When the septum of the nose is affected, the cartilage breaks down, the tip of the organ becomes depressed, and a stinking discharge escapes from the nostrils. In such circumstances breathing is very much interfered with, more especially if, at the same time, leprous deposit occurs or ulcerates in or about the glottis, the epiglottis, pharynx, tongue, or mouth generally. The senses of smell and taste are then lost for ever.

The eyes, also, are sooner or later attacked, lepromatous growth spreading from the conjunctiva on to the cornea or into the anterior chamber, or originating in the iris or ciliary body. Ultimately these organs also are destroyed.

6. *Sequelæ.*—Thus, in time, with the exception of that of hearing, one sense after another is lost. Ulcers form everywhere from the breaking-down of the nodules or from injuries to the insensitive skin. The cervical and inguinal glands, owing to leprous infiltration, swell and perhaps suppurate and become fistulous; the abdomen enlarges from leprous, perhaps combined with amyloid, infiltration of the liver, and there may be diarrhœa from amyloid disease of the intestine. In addition to these troubles, if the patient live, the nerve trunks are attacked. The fingers and toes ulcerate and drop off, or they become distorted and atrophied; or the phalanges are absorbed, the hands and feet becoming reduced to useless stumps. A peculiar goat-like smell is emitted by the ulcerating, decaying body. Altogether, the blind, lame, and unhappy wretch—still retaining his intellect, but devoid of every sense except that of hearing, breathing with difficulty through

Digitized by Google

a stenosed larynx, and racked by neuralgic pains and irregular outbursts of fever—comes to present, before the inevitable death from exhaustion occurs, a sadder, more loathsome, and more repulsive picture than anything imagination could conceive. Fortunately, in a large proportion of cases, the leper is mercifully carried off by phthisis, pneumonia, or some intercurrent affection at an earlier period, and before his disease can be said to have run its full course.

Nerve Leprosy.—Just as in nodular leprosy, in nerve leprosy the prodromal and macular stages may be severe, or slight, or altogether absent. Usually, however, in nerve leprosy much more frequently than in nodular leprosy, the ulterior and more distinctive lesions are preluded by a long and well-marked macular stage, during which large areas of skin are occupied by erythematous (Fig. 104), by pigmented, or by vitiliginous patches. The ringed form of eruption is a very usual one; a red, congested, slightly elevated and, perhaps, hyperæsthetic border enclosing a larger or smaller area of pale, anæsthetic, non-sweating integument—the whole resembling somewhat one of those extensive body-ringworms so common in natives of hot, damp climates, and for which these rings are sometimes mistaken. Such eruptions may come and go, or they may be permanent, or they may spread and multiply during many years before the more distinctive and graver signs of nerve leprosy are evolved.

A frequent and very distinctive symptom of this type of the disease, occurring often about this time, is the sudden appearance of bullæ (*pemphigus leprosus*)—one or more or a series of them—on the hands, feet, knees, backs of thighs, or elsewhere. These bullæ vary in size from a pea to an egg. After a few days they rupture, exposing a reddish surface which presently crusts over, exfoliates, and finally turns into a pale, perhaps anæsthetic spot with a sharply defined, pigmented border. More rarely the site of the bulla ulcerates. Should similar bullæ be formed in the neighbourhood of the first, the resulting ulcerations may unite into an extensive, probably superficial, serpiginous-looking sore.

A time comes when evidence of profound implication of the nervous system, in the shape of severe neuralgic pains, formication, hyperæsthesia, or anæsthesia, becomes more accentuated. The lymphatic glands enlarge, and there is often considerable fever with general distress. Hitherto the most prominent symptoms have been the skin lesions. These may remain or even increase; on the other hand, they may in part or entirely disappear. But whether the skin lesions increase or retrogress, evidences of

Digitized by Google

profound implication of the peripheral nervous system now distinctly show themselves; the neuralgic pains still further increase, and hyperæsthesia, anæsthesia, and various paræsthesiæ, along with

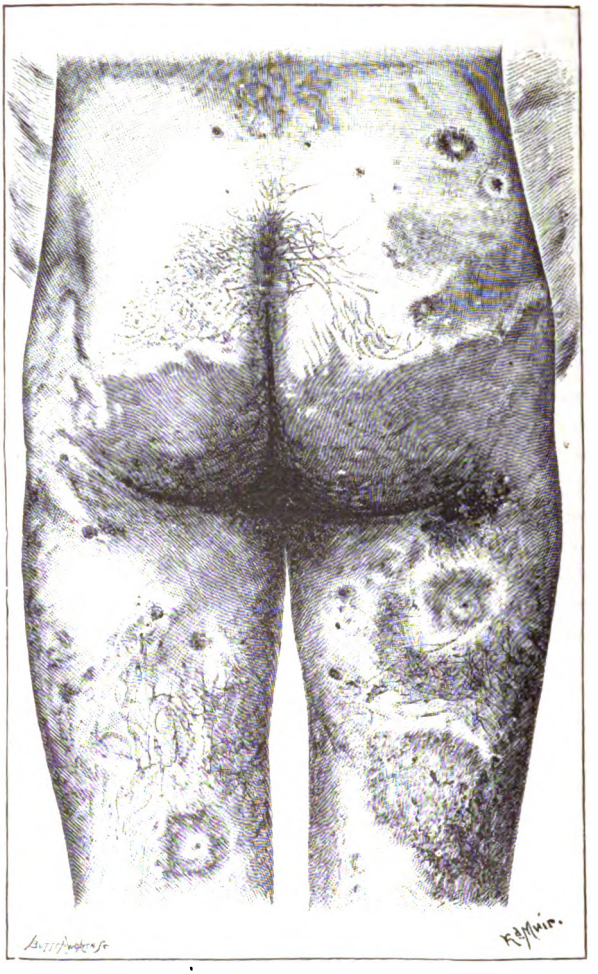


Fig. 104.—Nerve leprosy. (*After Leloir.*)

trophic changes in skin, muscle, and bone, the results of nerve destruction, become the dominating elements in the case.

If at this stage the ulnar nerve where it passes round the internal condyle of the humerus be examined, generally it will be found

Digitized by Google

to be the seat of a fusiform swelling, perhaps as thick as the little finger. Other nerves, such as the anterior tibial, the peroneal, more rarely the median, radial, brachial, and cervical nerves, especially where they pass over a bone and lie close under the skin, can be felt to be similarly swollen. Occasionally even the smaller nerves, where superficial, can also be detected hard and cord-like. At first these thickened nerves are tender on pressure, and the parts they supply may be the seats of hyperæsthesia and acute neuralgia. By degrees the great thickening of the nerve trunks decreases somewhat, the hyperæsthesia and neuralgia subside, and anæsthesia, paresis, muscular atrophy, and other trophic changes take their place. For a time the condition may fluctuate; the neuritis apparently may come and go with corresponding changes in the condition of the area subserved by the affected nerves. Sooner or later, however, fibrotic changes ensue in the neural leprous deposits, and the nerve tubules ultimately atrophy and disappear. The nerve tissue is now irreparably damaged, and trophic changes steadily advance. In other instances anæsthesia comes on without neuralgic pains, without hyperæsthesia, without constitutional symptoms, without discoloration of the skin, the patient discovering its existence by accident.

In nerve leprosy the anæsthesia begins most commonly in the feet, the thighs, hands, arms, forearms, and face. Later, and more rarely, it affects the trunk. The anæsthesia, though associated with well-marked lesions of the larger nerves, does not always, or even as a rule, coincide accurately with the anatomical distribution of their terminals—a circumstance which tends to show that the anæsthesia is not always and simply the result of lesion of nerve trunks, but that it may be the effect of the destruction by the bacillus of the nerve terminals themselves. This suggestion is strengthened by Gerlach's discovery that in anæsthetic leprosy the bacilli appear first in the skin around the nerve terminals, and only subsequently extend upwards to the nerve trunks. Another and sometimes a very striking fact in nerve leprosy is the symmetry observed in the distribution of some of the anæsthetic areas. This symmetry is by no means invariable; in not a few cases, however, it is very perfect and remarkable.

At the outset the anæsthesia in the affected patches may not be absolute; it may also come and go; and it may be very superficial, deep pressure being for a long time appreciable. But when the anæsthesia becomes, as it were, settled in a part, it seems gradually to extend deeper into the tissues; so that after a time it is absolute, and the part may be pinched, incised, and even

Digitized by Google

seared with fire, and the leper be absolutely unconscious of pain or even of being touched.

Step by step with the progress of the anæsthesia, atrophy of the subjacent muscles supplied by the thickened nerves proceeds. Along with the atrophy there is a corresponding distortion and a corresponding loss of power. There is no ataxia or inco-ordination of movement—simply feebleness. Thus the forearm wastes, the grasp is weakened, the thenar and hypothenar eminences and the interossei melt away, and the *main-en-griffe* or some such deformity is gradually produced (Fig. 105). Similar changes occur in the legs and feet, so that the power of walking is much impaired. The muscles of the thighs and upper arms, the pectorals, and the muscles of the face follow suit very much as in progressive muscular atrophy, only in the latter disease there is no superjacent anæsthesia.

Fig. 105.—Nerve leprosy: main-en-griffe. (*After Leloir.*)

In the affected nerve areas all the muscles are not simultaneously or equally attacked, so that, especially in the face, curious distortions may ensue. These facial atrophies, whether symmetrical or one-sided, in time produce a facies as characteristic of nerve leprosy as leontiasis is of nodular leprosy. Owing to muscular atrophy, the eyes, after a time, cannot be closed; the upper lid droops, the lower lid becomes everted, and the eye itself may become fixed. At first, owing to exposure of the organ, there is lachrymation; but by and by the secretion of tears dries up, the congested conjunctiva becomes cornified, the cornea ulcerates or turns leucomatous, and in the end sight is entirely lost. Ulceration often occurs in the mucous membrane of the nose, the septum being destroyed as in the nodular form; the tip of the nose may then fall down or be entirely lost. The lips, too, may become paralysed, thereby interfering with articulation and permitting the saliva to dribble from the mouth in a constant stream. Changes

Digitized by Google

occur, too, in the mucous membrane of the mouth; the gums may retract, exposing the maxillary bone, the teeth ultimately dropping out. Anæsthesia of the tongue and buccal mucous membrane, and implication of the muscles of mastication, may render eating and articulation very difficult.

In time the skin of anæsthetic patches on the limbs tends to atrophy; it loses its glands and hairs, and, in the end, may become so thinned and tense that it actually bursts into long cracks. The nails are not generally shed, but they become rough, or thinned, or atrophied into minute, hook-like appendages.

Ulcers form over exposed parts of the hands and feet. They may penetrate and disorganize the joints, and thus often cause fingers and toes to drop off, one after another. Or, perhaps, an abscess forms around a phalanx, destroys the periosteum, and ultimately leads to loss of the bone. Or a sort of dry gangrene may amputate finger or toe. Or there may be a curious interstitial absorption of one or more phalanges, the shaft of the phalanx wasting more rapidly than the articulating surfaces. In any of these ways the fingers and toes are distorted or destroyed. It is no unusual thing to see on a leper's hand a finger in which one or more of the phalanges have been thus got rid of without destruction of the fleshy part, or with only a general shrinking of this. Thus it comes about that a distorted, talon-like nail may crown a finger which is a mere stump; or, the finger having been entirely absorbed, the nail springs, as it were, directly from the knuckle.

Perforating ulcer of the sole of the foot, usually under the ball of the great toe or the heel, is a very common lesion in nerve leprosy.

On the whole, the advance of this form of leprosy is much slower than that of the nodular variety. The average duration of the latter is from eight to nine years, of nerve leprosy about eighteen years. Often such lepers live much longer—twenty, thirty, or even forty years. The end of these cases is quite as sad and repulsive as that of nodular leprosy. Death seldom results directly from the disease itself, but usually from diarrhœa, chronic nephritis, phthisis, pneumonia, or bronchitis.

MIXED LEPROSY.—As already explained, in most cases of nodular leprosy trophic changes from implication of nerve trunks ultimately supervene. Similarly, though not so frequently, nodular infiltration of the skin may appear in the course of what originally seemed to be a case of pure nerve leprosy. In yet other cases nodular and nerve lesions concur from the outset. In one or other of these ways what is known as mixed leprosy is produced. The lesions are in no way different from those already

Digitized by Google

mentioned, and therefore this form of the disease does not call for more detailed description.

Treatment.—Scrupulous and systematic attention to personal and domestic hygiene and cleanliness; frequent bathing and the free use of soap; frequent changes of underclothing; good food; fresh air; light work; the avoidance of overstrain, fatigue, and of exposure to bad weather—these things are all of prime importance in the treatment of leprosy, and should be insisted on. It has been found that most lepers on being placed in favourable hygienic conditions improve for a time, and that in a small proportion of cases the disease by these means may sometimes be actually arrested. Europeans who have contracted leprosy in the tropics almost invariably undergo temporary improvement on return to the more bracing climate and more nutritious diet of their native lands. It seems to us that the methods of treatment now coming into vogue for tuberculosis are equally applicable to leprosy.

Many drugs have been regarded, from time to time, as being more or less of the nature of specifics in the treatment of this disease. But, though some of these drugs appear for a time to do good, and in consequence acquire a certain degree of popularity, hitherto all of them, one after another, have sooner or later fallen into disfavour. One is very apt to be deceived in estimating the value of a drug in leprosy. The leper applies for treatment generally during, or soon after, one of the periodical exacerbations of the disease, and when the nodules and other eruptions are active and well pronounced. In the natural course of events, and without treatment of any description, especially if the patient be placed under favourable hygienic conditions, these acute manifestations tend to become quiescent, and the disease temporarily to ameliorate. Observers are too apt to attribute this natural and temporary amelioration to whatever drug the patient may happen to be given at the time. Moreover, in judging of the value of any drug in leprosy, it must be remembered that the disease may be arrested spontaneously, or even be recovered from, without the use of any drug whatever.

Chaulmoogra oil (*oleum gynocardium*, obtained from the seeds of *Taraxtogenos kurzii*), in doses of from 2 to 10 up to 40 drops or more, according to tolerance, three times a day, together with inunction of the same drug mixed with some oil, is a favourite remedy with English practitioners. Such lepers as can assimilate large doses of this drug appear to derive benefit. Sandwith has reported a case in which marked benefit followed persistent

Digitized by Google

hypodermic administration of chaulmoogra. Manson had lepers under his care who, in addition to large doses of chaulmoogra by the mouth, received hypodermic injections daily up to one drachm of the drug. The improvement for a time was marked. The bacilli, however, were just as abundant in the nodules during and after as before treatment, and there was no alteration in their appearance. Encouraged by the clinical results, he persevered with this treatment for many weeks at a time. In one instance the patient died from what was suspiciously like fat embolism; in another, while very large doses of chaulmoogra were being taken by the mouth and injected hypodermically, severe leprotic fever, associated with profuse eruption of lepromata, set in. In 1890 Dr. Z. Roux pointed out that gynocardic acid and gynocardates of soda and magnesia could be obtained from chaulmoogra, and were better borne. Heiser first suggested the method of subcutaneous injection, and since then Sir Leonard Rogers has obtained very encouraging results from the intravenous injection of *sodium gynocardate* * in doses of $\frac{1}{10}$ to $\frac{4}{5}$ gr. in 3-per-cent. sterilized solution. A definite local reaction in a proportion of cases, sometimes with fever, follows the injection, and Rogers believes that actual destruction of the organisms in the lepromata can be demonstrated. It is important to inject gynocardates free from palmitic acid, very little pain or swelling then being produced at the site of injection. For intramuscular dosage a minimal dose of 2 c.c. (4 gr.) of sodium gynocardate solution is recommended; the maximum being 12 c.c. or 24 gr. given twice weekly.

Latterly *sodium morrhuate* has been advantageously combined with the gynocardate. The following scheme of intensive treatment is recommended by Muir:—

First Week.—Sodium gynocardate "A" (known also as sodium hydnocarpate) 0·5 c.c. intravenously, first day.
Sodium gynocardate "A" 0·25 c.c.; sodium morrhuate 0·25 c.c., third day.
Sodium morrhuate 0·5 c.c. intramuscularly, fifth day.

Second Week.—Sodium gynocardate "A" 1 c.c. intravenously, first day.
Sodium gynocardate "A" 0·5 c.c.; sodium morrhuate 0·5 c.c., third day.
Sodium morrhuate 1 c.c. intramuscularly, fifth day.

This dosage to be increased by 0·5 c.c. week by week up to 5 c.c., provided there is no marked febrile reaction or other danger signal.

The consensus of opinion at present appears to be that in the gynocardates we possess an agent superior to all others hitherto

* The drug, put up in proper doses in ampoules, can be obtained from Messrs. Smith, Stanistreet & Co. Two salts of gynocardic acid are present—sodium gynocardate and sodium hydnocarpate.

Digitized by Google

employed in leprosy. Rogers has recorded that in the treatment of 51 cases by this method no fewer than 14 have remained free from signs of the disease for the last two and a half years. Soya bean oil, being less irritating than the gynocardates, is now receiving a trial.

Tuberculin has been tried. It produces a local and a general reaction, which is sometimes curiously delayed for one or two days. So far from doing good it seems to aggravate the disease, causing fresh eruptions, and also causing bacilli to appear in the blood.

Iodide of potassium aggravates leprosy if given in full doses; it not only affects the general health prejudicially, but it causes fresh eruptions to appear.

Manson tried thyroidin in a case of nerve leprosy. The patient remained absolutely free from symptoms for many years and until lost sight of.

When leprous nodules spread on to the cornea and threaten to interfere with the line of vision, Brockmann has shown that the extension of the leproma may be arrested by division of the cornea on the pupillary side of the lesion; it is found that the bacilli do not traverse the cicatrix. Tarsorrhaphy for ectropion of the lower lid, iridectomy for iritis or synechiæ, tracheotomy for laryngeal stenosis, and necrotomy for bone disease, may sometimes have to be performed. Horder strongly recommends amputation for perforating or other forms of leg ulceration; the general health is much improved by the removal of such sources of sepsis. The existence of leprosy does not materially interfere with the success of surgical operations. Manson once removed an enormous elephantiasis of the scrotum from a confirmed leper; the presence of the leprosy did not prevent sound healing of the extensive operation wound, the man making a good recovery so far as the operation was concerned.

If only one tubercle or one limited lepra macula is present, and there have been no constitutional signs of a general invasion, it is advisable to excise freely the affected spot.

What promised at one time to prove an important advance in the therapeutics of leprosy is the method introduced by Deycke under the name of *nastin* treatment, but recent reports do not support the claims originally made for it. Similar preparations, such as Williams's vaccine and Rost's "leproline," are on trial.

Prophylaxis.—The leper must be regarded as a source of danger, and, *qua* leprosy, the only source of danger, to any community he may live amongst. Therefore a sure and the most effectual way of suppressing the disease is the thorough isolation

Digitized by Google

of existing lepers. There are many difficulties, however, especially in such countries as India, in giving practical expression to what appears to be a perfectly logical conclusion—difficulties springing from the rights of the individual, finance difficulties, difficulties arising from concealment or incorrect diagnosis, as well as from the continued introduction of fresh cases from without. These and other obvious obstacles, incident to any attempt at a wholesale system of thorough isolation, are so great that the most that can be hoped for at the present time, and in the present state of public opinion, is some modified system of segregation and isolation, such as that which has worked so successfully in recent years in Norway.

Where possible, therefore, lepers should be segregated in isolated asylums, which should be so conducted as to prove attractive. Those who cannot be made, or persuaded, to enter these asylums should be isolated as much as possible from their families and the public; scrupulous cleanliness of their persons and houses should also be insisted on. Lepers ought not to be allowed to beg in the streets—as is often the case in Eastern cities—to keep shops or to handle food or clothes intended for sale, to wander about the country as pedlars or mendicants, to hire themselves out as servants or prostitutes, or to frequent fairs and public places. All lepers in the ulcerative stage of the disease, when it is to be presumed that myriads of bacilli are being constantly given off from their sores, should be still more scrupulously isolated, their discharges, clothes, and dressings being systematically destroyed or disinfected. A child born of a leper should at once be removed from the diseased parent, and, if necessary, cared for at the public expense.

Leprosy is feebly contagious, or, rather, the conditions for successful contagion rarely occur; so rarely, that it is more than probable that, under such a modified system of segregation and isolation as that indicated, they would occur so seldom that the disease would rapidly die out.

Vaccination.—It has not been actually proved that leprosy can be communicated by vaccination, although there is some evidence in favour of such a supposition. But, although this has not been proved, it is an obvious and very desirable precaution, in countries in which the disease is endemic, to take care that the vaccinifer is not only not the subject of actual leprous eruption, but also that he or she comes from a family and community free from leprosy. An apparently healthy vaccinifer may contain lepra bacilli in a latent state—may be, in fact, a potential leper and capable of communicating the disease.

Digitized by Google

CHAPTER XXXVII

YAWS (FRAMBŒSIA)

Synonyms.—Pian; Frambœsia; Boubas (Brazil); Coko (Fiji); Parangi (Ceylon); Dube (Gold Coast).

Definition.—Yaws is a contagious inoculable disease characterized by an indefinite incubation period followed usually by fever, by rheumatic-like pains, and by the appearance of papules which generally develop into a fungating, encrusted, granulomatous eruption. It runs a chronic course; is mostly protective against a second attack; is believed to be caused by *Spironema pertenue* vel *pallidulum;* is amenable to salvarsan and, to a certain extent, is influenced by mercury and potassium iodide.

Geographical distribution.—Yaws is widely diffused throughout the greater part of the tropical world. In certain places it is very common—as in tropical Africa, particularly on the west coast; in many of the West India Islands; in Ceylon, in Fiji, Samoa, and many of the islands of the Pacific; in Papua; in Java, Sumatra, and the Malay States. It is difficult to say to what extent it exists in India; some deny its presence there altogether, but Powell has recognized and described it as occurring in Assam. The disease known as "purru" in the Malay Peninsula is probably yaws. In China yaws is rare—at all events on the coast. In some of the West India Islands, and Fiji, almost every child passes through an attack. In the latter, according to Daniels, those children who do not acquire the disease in the ordinary way are inoculated with it by their parents, who regard an attack of yaws as an occurrence more or less necessary and wholesome.

It is impossible at the present day to settle the point, but it seems probable that yaws was originally an African disease, and, so far as America and the West Indies are concerned, that it was introduced by negro slaves. In the days of West Indian slavery the specific and infectious nature of yaws was thoroughly recognized. The planters controlled it by instituting yaws-houses and similar measures, but since the emancipation of the negro the disease has again become very prevalent. Yaws is practically confined to the tropics and subtropics, and even there is absent

Digitized by Google

at high altitudes, but, owing to its great similarity to syphilis, and the extent to which these two diseases overlap, it would appear to be impossible to define its exact limits. Probably some reciprocal immunity between the two diseases exists, for wherever yaws is widespread—as, for instance, in the Pacific islands—there syphilis appears to be unknown.

Etiology. *Contagion and heredity.*—As yaws is highly contagious, all circumstances favouring contact with the subjects of the disease favour its occurrence. Simple skin contact does not suffice; a breach of surface is necessary. Probably the virus is often conveyed by insect bites, or by insects acting as go-betweens and carrying it from a yaws sore to an ordinary abrasion, wound, or ulcer. Thus the disease often commences in a pre-existing ulcer. Cases are prone to originate in certain dirty houses, the virus from previous yaws patients seemingly impregnating the floors and walls of the filthy huts in which the latter had resided. In this manner the disease may be, and in some cases no doubt is, acquired without direct transference from an existing case.

Yaws is neither hereditary nor congenital. A pregnant mother suffering from yaws does not give birth to a child suffering from the same disease, nor one which will subsequently develop yaws unless the virus be first introduced directly through a breach of surface after birth. It is not conveyed by the milk; nor does a suckling suffering from yaws necessarily infect its nurse. On the other hand, yaws is most frequently conveyed by the mother, suffering from a secondary eruption, to her otherwise healthy child.

Although two-thirds of the cases in the West Indies occur before puberty, no age is exempt. Three males are infected to every female. Neither occupation nor race has any manifest influence.

In 1905, by overstaining with Giemsa's stain, Castellani demonstrated in scrapings of yaws tissues the presence of an extremely delicate treponema, *Spironema pertenue* (*S. pallidulum*), very like that of syphilis. Castellani's observations have been amply confirmed.

To demonstrate the spironema, slides should be prepared from scrapings of an incised yaw papule before it has ruptured. The films may then be stained with Giemsa, or by the indian-ink method; better still, the living parasites may be detected in fresh undried films by the dark-ground illumination. A fully developed yaw is unsuitable, because, in consequence of its having been exposed

Digitized by Google

to external sources of contamination, a variety of organisms will be present and may confuse the observer. Opinions differ with regard to the exact morphology of *S. pertenue*, but later observers, including Dobell, have been unable to distinguish any structural differences between this spironema and *S. pallidum* of syphilis (Fig. 65, 5, p. 212). Granule-shedding has been watched with the microscope, and may possibly constitute an evolutionary stage in the life-history of the parasite.

S. pertenue has been found in the spleen, lymphatic glands, and bone-marrow, and doubtless it occurs in the blood. It is inoculable into monkeys and rabbits; in the former, especially in the orang-outang, it gives rise to lesions similar to those met with in man.

By aspirating gland-juice Nicholls has succeeded in infecting rabbits by the intratesticular route; Castelli has produced the secondary eruption by the intravenous route. The disease was originally reproduced in the big apes in Sumatra by Neisser, Baermann, and Halberstädter, who found no reciprocal immunity in these animals when subsequently infected with syphilis; but this view is opposed to the work of Levaditi and Nattan-Larier.

Cultivation of *S. pertenue* has been successfully performed by Noguchi in ascitic fluid containing a piece of fresh animal tissue such as the kidney, the whole being covered with a layer of sterile paraffin. This rather complicated technique has been simplified by the later work of Hata, who substituted horse-serum, the inoculation being made through the upper solidified layer. To succeed in the cultivation of these spironemata strict anaerobiosis is necessary.

Symptoms.—As in syphilis, the symptoms of yaws can be divided into three stages, primary, secondary, and tertiary, while late sequelæ comparable to parasyphilitic lesions of the central nervous system have been described by Harper in Fiji.

Primary stage.—In yaws there is an incubation stage of very variable duration—two to three weeks; in experimental apes it may be as long as three months. Naturally-acquired yaws is reputed to have a longer incubation period than the inoculated disease. The primary lesion may appear as an isolated papule or a bulla, developing a few days later into an undermined ulcer with a raw base. It is always extragenital and may be situated on any part of the body. It may be so small as to escape detection; in fact, great difficulty may be experienced in differentiating it from many allied cutaneous lesions. It may be added that many good observers deny the existence of a primary sore in yaws.

The appearance of the lesion is preceded by a certain amount of constitutional disturbance. The intensity of the general symptoms varies within wide limits. Sometimes they are hardly

Digitized by Google

perceptible, and are not complained of; usually there is well-marked malaise with rheumatic pains. Occasionally there is severe constitutional disturbance, lasting for about a week, with rigor, smart fever (100° to 103° F.), persistent headache, pains—worse at night—in the long bones, joints, and loins, and sometimes gastric disturbance and diarrhœa, especially in children. During the decline of these constitutional symptoms the eruption appears.

Secondary stage.—This is ushered in by a fine, light-coloured furfuraceous desquamation, originally described by Nicholls. The skin becomes harsh and dry, loses its natural gloss, and here and there the patches of desquamation, best appreciated with the aid of a lens, are formed. These patches are mostly small and circular; occasionally they are oval, irregular, or form rings encircling islets of healthy skin. They are scattered irregularly over limbs and trunk; occasionally they may be almost confluent, the patches coalescing and giving rise to an appearance as if the entire skin had been dusted over with flour. On the other hand, this furfuraceous desquamation may be so slight as to be overlooked. In other instances it may be very marked, the heaping up of desquamating epidermic scales producing white marks, very evident on the dark skin of a negro or oriental.

This patchy, furfuraceous condition of the skin occurs not only at the early stages of yaws, but may persist throughout the attack, or reappear as a fresh eruption at any period of the disease.

Appearance of the yaw (Fig. 106).—When the furfuraceous patches have been in existence for a few days, minute papules appear in them. This very characteristic eruption, from which the disease takes one of its names—framboesia (or raspberry)—breaks out three months after the primary lesion. As in syphilis, the eruption may be very pleomorphic; it may be a roseola or consist of macules with desquamation resembling a squamous syphilide. It may appear on any part of the body, especially in exposed situations and on the anterior surface. The papules (Fig. 107) occur in groups, the larger appearing to be surrounded by a group of satellites, which has given rise to the appellation "mamanpian" ("mother yaws"). Auto-inoculation is probably responsible for the appearance of these lesions in symmetrical fashion whenever the skin or mucous surfaces come into intimate contact; they are present at the angles of the mouth, in the axillæ, in the anal cleft, and in the inguinal region; in contradistinction to syphilis, they are rarely present on the true mucous surfaces, but often in clusters just inside the nostril. Several

Digitized by Google

of the groups may coalesce to cover a large surface. An individual yaw may be no larger than a pea, or may attain the size of half a crown.

According to Nicholls, they are apparently pushed up from the rete Malpighii through the horny epidermis, which breaks

Fig. 106.—Secondary rash of yaws. (*By permission of Dr. Sambon.*)

over their summits and splits in radiating lines from the centre, the necrosed segments curling away from the increasing papule. Soon a yellow point appears around a hair-follicle, consisting of a cheesy-looking substance, which cannot be wiped away unless undue force be used.

Digitized by Google

The papule, having arrived at this stage, may either cease to grow, the apex becoming depressed, or it may go on to the formation of the typical yaw. In the latter case the lesion gradually grows into a rounded excrescence, the yellow material at the top widening out so as to form a complete cap encrusting the little tumour. The smaller tumours are hemispherical; the larger are more flattened or even depressed at the centre, possessing everted, somewhat overhanging, rounded edges. Occasionally, though rarely, a big yaw may include an area of sound skin.

The firmly adherent crust which caps and encloses an uninjured yaw is yellowish, granular, blotched with blood-stains

Fig. 107.—Case of yaws. ("*Journ. Trop. Med.*")

and encrusted dirt. Deprived of its crust the little swelling is seen to be red in colour, and generally smooth and rounded on the surface, and oozes pale yellowish serum, in which spironemata may be demonstrated; when inspissated, this serum forms a fresh cap to the yaw. According to size, it stands out anything from $\frac{1}{8}$ to $\frac{2}{8}$ in. above the surrounding healthy skin. Pus, unless as a consequence of irritation, is not, as a rule, found under the crust.

Although the formation of the papules and yaws is attended with much itching, the yaw itself is not at all sensitive; the tumour may be touched, with acid even, without causing pain—a diagnostic point of some importance. Sometimes, as in syphilis, the eruption has a circinate character, the so-called "ringworm yaws."

Digitized by Google

The yaw usually attains its maximum development in two weeks. For several weeks longer it remains stationary before beginning to shrink. The crust then thins, shrinks, darkens, separates at the periphery, and at last falls off, disclosing at the site of the former fungating mass a slightly thickened spot of fairly sound skin which, though pale at first, may subsequently become hyperpigmented. Histologically, the individual yaw consists of hyperplasia of the true epidermis and formation of granulation tissue; giant cells may be present.

Simultaneously with the appearance of the eruption, as in secondary syphilis, there is a uniform, painless enlargement of the lymphatic glands, in the aspirated lymph of which the organism may be demonstrated. It can also be demonstrated in the skin lesions by Levaditi's silver impregnation method.

The serum of patients in the secondary stage gives a marked positive Wassermann reaction, thus making the differential diagnosis from syphilis, by that means alone, impossible.

Tertiary stage.—It sometimes happens that the tumours, in place of becoming absorbed, break down and ulcerate, the ulceration, however, which may last for years, being confined to the yaw itself. In other instances ulceration goes deeper and extends circumferentially, giving rise to extensive sores with subsequent cicatricial contractions. Such ulcerations occur in about 8 per cent. of cases, and may or may not be encrusted. With the development of the deeper and wider forms of ulceration the typical lesions of yaws may disappear for a time, or perhaps permanently. In the latter case the ulcers are said not to be infective, and do not communicate yaws. Ulceration of the greater part of the limbs, especially the leg and ankle, may take place.

Lesions of the hands.—A scaly condition of the palms of the hands may persist for years. A multiple dactylitis, with uniform swelling of phalanges, atrophy of the nails, and subsequent deformity, is often observed. Yaws may occur around or under a nail and give rise to a troublesome form of onychia.

Foot yaws.—When a yaw develops on the sole of a foot, in consequence of being bound down by the dense and thick epidermis it causes much suffering. Spreading laterally under the thick, leathery, and unyielding epidermis, it may attain a large size. After a time the epidermis over the growth gives way, splitting in a radiating fashion (Fig. 108). Pressure being thus removed, the yaw fungates, and suffering diminishes.

Gangosa or *destructive ulcerous rhino-pharyngitis* (Fig. 109), which has been regarded by some as a sequel of yaws, generally commences

Digitized by Google

as an ulcer on the soft palate. Slowly spreading, it may make a clean sweep of the hard palate, the soft parts, cartilages and bones of the nose, sparing the upper lip, which is left as a bridge across a great chasm, the floor of which is formed by the intact tongue. A most offensive odour is given off from the ulcerated surface. The disease may be arrested spontaneously at any period of its progress and long before so extensive a mutilation as that described has been effected ; but it is always a long-standing and chronic affair and may linger as an indolent ulceration for years. As a rule, the larynx is spared ; but, although phonation may be retained, articulation is seriously impaired. Gangosa occurs at any age, but is rare

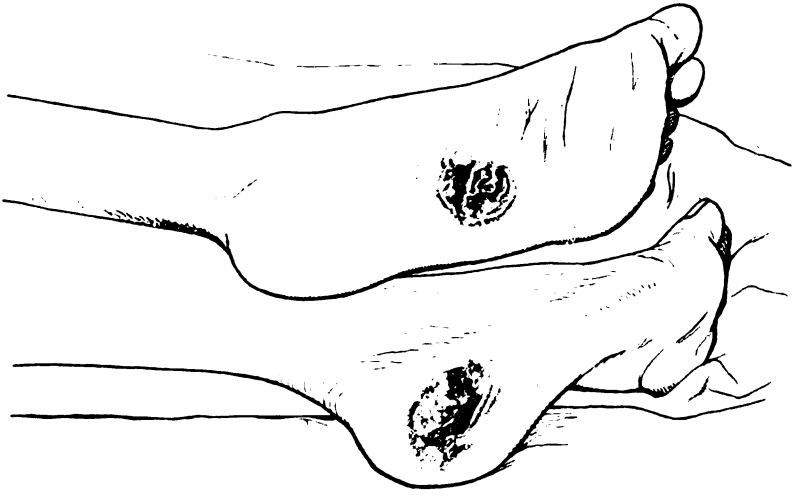


Fig. 108.—Foot yaws. (*After Terzi ; by permission of Dr. Sambon.*)

in young adults, though Leys states that in Guam he has seen it in children of 3, 4, and 9 years of age. It is very common in parts of the West Indies—Dominica for example (60 cases in a population of 2,000), Guam (1·5 per cent. of population), the Carolines, Fiji, British Guiana, and undoubtedly many other parts of the tropics.

The lesion has been attributed to leprosy, tuberculosis, syphilis, and yaws. There is no satisfactory evidence that it is due to any of these diseases. Against its being syphilis is the practical absence of syphilis among the natives of Fiji and Guam, where this form of ulceration is particularly common, and other syphilitic stigmata are unknown. It is stated that the serum gives a positive Wassermann reaction, and positive luetin phenomena have been observed

Digitized by Google

after artificial inoculation; but this reaction is obtained in yaws, trypanosomiasis, and other non-syphilitic diseases. Against its being a sequel of yaws is the want of correspondence in the proportional prevalence of the two diseases; for, although ulcerative rhinopharyngitis is common in some places in which yaws is common, it is said to be rare in other places where yaws is common, and common in other places where yaws is rare. The cases the Editor has personally observed were associated with tertiary yaws-scars on other parts of the body.

Fig. 109.—Gangosa in a Sinhalese. (*Orig.*)

It has been suggested by Leys that gangosa is a disease *sui generis;* there is no conclusive evidence for this at present. On the other hand, it is not a form of buccal leishmaniasis.

Duration and recurrences.—Yaws lasts for weeks, or months, or years, its duration depending on the general health, idiosyncrasy, hygienic conditions, and the treatment employed. Mild cases in healthy subjects finish in about six weeks; the average duration of an attack of yaws is estimated at about one year. In other instances, especially in the debilitated, the disease runs on for months, successive crops of eruption being evolved. Sometimes these recurrences may stop short at the stage of desquamation,

Digitized by Google

or at the papular stage, or they may proceed to the formation of typical yaws. The recurrences are usually preceded by feverishness, pains in the bones and joints; and the successive crops may either be limited and partial in their distribution, or they may be general.

Periostitis, osteitis, and epiphysitis (Figs. 110, 111, 112).—Circumscribed painful periosteal nodes are frequently met with on the anterior aspect of the long bones, especially the radius, ulna, and tibia. The swellings are hot and exquisitely tender, and the

Fig. 110.—Distortion of fingers in tertiary yaws. (*Orig.*)

superjacent skin is tense and stretched. After the subsidence of the acute stage, hard long periosteal nodes remain. A diffuse osteitis may result in a sabre-shaped deformity of the bones exposed to pressure, especially the tibia, though one has seen it almost equally well marked in the arms and fingers. A rarefying process is also at work, for such bones are subject to spontaneous fracture with resulting malunion. Such accidents are of common occurrence in those districts in which yaws is endemic. A chronic periostitis of the clavicle is of frequent occurrence in Fiji. Possibly the "goundou" of Africa is a sequel of yaws, as has been suggested. These bone changes are accompanied by intense

Digitized by Google

rheumatic pains, and have received distinctive names, such as "sasala" (Fijian).

Synovitis.—A chronic synovitis, analogous to that of tertiary syphilis, often associated with bone lesions and, it may be, with disorganization of the joint, has been noted.

The general health.—Except during the initial fever, or

Fig. 111.—Tibial periosteal nodes, ulcers, and deformity of phalanges in yaws. (*Orig.*)

during one of the recurring febrile relapses, the general health is not, as a rule, affected. Occasionally, however, there is debility and cachexia; or there may be enlargement and tenderness of the lymphatic glands. In other instances the rheumatic pains are a principal feature and may be very severe.

Sequelæ.—Mention has been made of nodes, of gummatous-

Digitized by Google

like thickenings, and of punched-out, serpiginous, and lupoid ulcerations in connection with yaws. Chronic serpiginous ulcerations of the forearms and legs, which, subsequently cicatrizing, lead to constriction, and cause unsightly chronic œdematous swelling of the distal parts; the gumma-like lumps on arms and

Fig. 112.—Sabre-like deformity of tibia, radius, and ulna, and multiple cutaneous ulcerations, in yaws. (*Orig.*)

legs, and even on the lips, especially the lower lip, causing a permanent enlargement, must also be mentioned. Harper brings forward evidence showing that in Fiji, at any rate, late manifestations comparable to parasyphilis exist, in the shape of aneurysm, general paralysis of the insane, and locomotor ataxia.

Mortality.—Although in the literature of the subject reference

Digitized by Google

is made to deaths from yaws, yet, judging from the statistics collected by Nicholls, the mortality must be very small indeed. In 7,157 West Indian cases, treated in various yaws hospitals, there were only 185 deaths—a mortality of 25·8 per thousand; a death-rate, as Nicholls points out, less than the average annual death-rate in one of the islands—Antigua. Doubtless, although yaws itself seldom proves directly fatal, intercurrent diseases, such as sloughing phagedæna and phagedænic ulceration, predisposed to by the skin lesions, occasionally do so.

Morbid anatomy and pathology.—No visceral changes have been found peculiar to yaws, although, of course, when yaws concurs with syphilis, gummata, etc., may be found; in this case the concurrent gummata may belong to the syphilitic and not to the yaws infection. An important point of contrast in the respective morbid anatomy of yaws and syphilis is the absence of endarteritis in the former and its frequency in the latter.

Diagnosis.—A painless, insensitive, larger or smaller, circular, encrusted, red, granulomatous excrescence occurring in an endemic district is almost certainly yaws. The most important point in connection with yaws, as regards both diagnosis and etiology, is its relationship to *syphilis*. It has been, and is still, held by some distinguished authorities that yaws is syphilis modified by race and climate. Certain features which the two diseases have in common are pointed to, and doubtless the discovery of spironemata in association with both diseases will be adduced in support of this contention. So far as clinical and macroscopical evidence goes, it is decidedly in favour of, not to say conclusive for, regarding the two diseases as specifically distinct. There are many points of contrast in their clinical features. We may mention the primary sore, the infection of the fœtus, the more pronounced adenitis, the exanthem, the alopecia, the absence of itching, the iritis, the affection of the permanent teeth, the eye affections, the congenital lesions of syphilis; all these are wanting in yaws. Moreover, both diseases may concur in the same individual (Powell cites two cases, and Charlouis two, of syphilis supervening on yaws); and antecedent syphilis certainly does not confer immunity as against yaws, nor antecedent yaws against syphilis. The serum of both diseases gives a positive Wassermann reaction. Monkeys inoculated with yaws are not absolutely immunized against syphilis, but Prowazek found under experimental conditions that inoculation of the spironema of yaws conveys a relative immunity to a subsequent syphilitic infection, and that monkeys were less susceptible to syphilis after a previous attack of yaws. Yaws may die out in

Digitized by Google

a community, as in British Guiana (Daniels), yet syphilis remain; yaws may be universal in a community, as in Fiji and Samoa, and yet true syphilis, whether as an acquired or a congenital disease, be unknown. Finally, syphilis has never been shown to give rise to yaws, nor yaws to syphilis; neither, so far as known, has yaws been evolved in any community from syphilis, or appeared independently where the possibility of its having been introduced from a recognized yaws centre could be excluded with certainty.

The therapeutic argument for the identity of the two diseases is a very fallacious one. Sulphur will cure scabies and pityriasis versicolor; yet from this circumstance we may not conclude that these diseases are identical. The same may be said in respect of the influence of salvarsan, mercury, and iodine on syphilis and on yaws.

The secondary furfuraceous eruption has to be distinguished from the dermatomycoses—*tinea albiginea* and *tinea circinata*—and the tertiary ulceration from ulcus tropicum and blastomycosis of the skin.

Prophylaxis resolves itself into the adoption of measures to prevent contagion. These are: the isolation and segregation of the affected; the dressing and treatment of wounds in the hitherto unaffected; the application of antiseptic ointments to yaws sores, so as to obviate the diffusion of germs; the purifying or destruction by fire of houses or huts notoriously infected; the prevention of pollution of bathing-water by yaws discharge; and, especially, the prompt treatment by salvarsan, etc., of the infected.

Treatment.—All are agreed as to the propriety of endeavouring by good food, tonics, and occasional aperients to improve the general health. Most are agreed as to the propriety of endeavouring to procure a copious eruption by stimulating the functions of the skin by warm demulcent drinks; by a daily warm bath with plenty of soap; and, during the outcoming of the eruption, by such diaphoretics as liquor ammoniæ acetatis, guaiacum, etc. Warm clothing is indicated. Except where much bone destruction has taken place, salvarsan or, better still, its more recent and more soluble derivatives have an almost magical curative effect upon yaws in every stage of the disease. The most generally used drug at the present time is *novarsenobillon*. It is given intravenously to adults and, if possible, to children; or intramuscularly (0·4 grm. dissolved in oil, into the buttock). The more urgent symptoms yield much more rapidly than in syphilis, and relapses are uncommon. For adults the dosage advocated is 0·9 grm., for young adults 0·6 grm., for children up to 10 years

Digitized by Google

of age 0·3 grm., and for children under 2 years 0·1 grm. The reader is referred to p. 184 for a description of the technique of administration. Some believe that the majority of cases do not require more than one injection.

The systematic use of salvarsan in a yaws community would, if thoroughly carried out, promptly get rid of the endemic, and, wherever possible, should be enforced. The recent Colonial Office reports have emphasized its value from an economic point of view. The average time to effect a cure is given as eleven days.

Many practitioners use mercury, or potassium iodide, or both, after the eruption is fully developed. These drugs have undoubtedly the power of causing the eruption in yaws to resolve. Atoxyl has no action on yaws. In Ceylon the intravenous injection of 3–5 c.c. of standard solution of mercury and arsenious iodide (liq. arsenici et hydrargyri iodidi) has been followed by good results; it is slower in action but cheaper than salvarsan, and may be used as a substitute for that drug in times of stress.

During convalescence iron, arsenic, and quinine are indicated.

Digitized by Google

CHAPTER XXXVIII

OROYA FEVER AND VERRUGA PERUVIANA

UNTIL the work of the Harvard Commission under Strong in 1914 was published, Oroya fever and verruga Peruviana were considered to be but different clinical manifestations of the same disease. The prevalent idea was that the former constituted the initial stages of verruga; further, that, should the patient survive the very severe initial pyrexia, he would later develop the eruption characteristic of verruga. This theory was disposed of by Strong's inoculation experiment, in which a volunteer was inoculated with extracts of verruga lesions, and sixteen days later developed typical verrucose lesions without any preliminary pyrexia or the anæmia so characteristic of Oroya fever. Strong is, however, of the opinion that as these two diseases, so dissimilar in every way in their clinical manifestations, are endemic in the same localities, they may often coexist in the same individual. Though probably of an entirely distinct etiology and pathology, Oroya fever and verruga Peruviana are considered together on account of their intimate historic and other associations.

OROYA FEVER (CARRION'S DISEASE)

Definition.—An acute specific fever, of which the etiology is still uncertain, endemic in certain valleys of the Andes, and characterized by a rapidly developing anæmia of the pernicious type, irregular pyrexia, and great tenderness over the blood-forming tissues.

Geographical distribution.—Between the 9th and the 16th parallels of S. latitude, and at an elevation of from 3,000 to 10,000 feet, in certain narrow valleys of the western slopes of the Andes this peculiar fever is endemic. Its topical as well as its geographical range is singularly limited; it is confined to certain hot, narrow valleys or ravines, the inhabitants of neighbouring places being exempt.

It is said that the disease may be acquired in merely journeying through the endemic districts, more especially if the traveller passes the night there.

Etiology.—Although out-of-door workers are the most subject,

Digitized by Google

all ages, classes, and both sexes, including infants, are liable to attack.

The fatal experiment of Carrion, who, in 1885, inoculated himself with the virus of the lesions of verruga Peruviana, was thought at that time to prove that the latter disease was communicable; a month later he died of the disease now known as Oroya fever. As a result of this experiment it was believed that verruga material would cause an initial fever, which was henceforward popularly known as Carrion's disease. During the fever certain rod-like bodies are to be found in a large proportion of the red

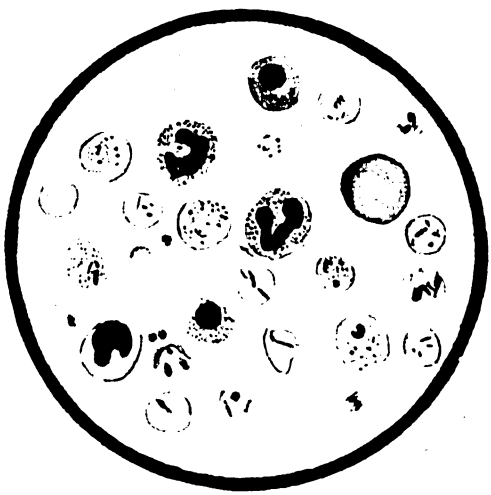


Fig. 113.—Blood-film in Oroya fever, showing bacilliform bodies in red cells. × 800. (*Partly after Schilling.*)

blood-corpuscles (Fig. 113), and in endothelial cells of the lymphatic glands. These were first noted by Barton in 1909, and were considered by him to be protozoal in origin; these findings were subsequently confirmed by Strong and other members of the Harvard Commission, and the bodies were termed by them *Bartonella bacilliformis.* Strong regards them as Protista, allied to Grahamella, and the cause of the disease. They somewhat resemble stages of a piroplasm (*Theileria parva*) during its cycle in the lymphatic glands. They may be so numerous that no field, as seen under the oil-immersion lens, is free from infected cells. Two forms are recognized—one is a rod-shaped, slightly curved bacillary organism 2 μ long by 0·5 μ broad, staining with Romanowsky an intense

Digitized by Google

blue, often in branching forms and in chains, but never crossed; the other form is a rounded body about 1 μ or less in diameter, usually oval or pear-shaped, and containing chromatin granules. Both forms are difficult to distinguish in fresh blood, and show feeble independent movement. So far, it has been impossible to convey the disease to laboratory animals by injection of blood.

Paratyphoid and other coliform organisms have been cultured from the blood by Barton and others, but are not the true cause of the disease.

The disease is most prevalent from January to April, when the streams are in flood, the air hot, still, and moist, malaria epidemic, and insect life abundant. An insect transmitter is suspected, but not yet determined. Townsend, who has made special studies on this point, dismisses ticks, bugs, and the ordinary human ectozoa, and inclines to regard a species of phlebotomus as the carrier.

Pathology.—A remarkable feature of this disease is the rapidity and extreme degree of blood destruction. In bad cases the blood-count may drop in three or four days to 500,000 per c.mm., the picture being that of a pernicious anæmia. There is a marked polymorphonuclear leucocytosis with disappearance of eosinophils; and during the later eruptive stage an eosinophilia with a mononuclear leucocytosis.

In addition to the anæmia, marked changes are present in the liver, spleen, and bone-marrow. In the liver, areas of degeneration and central necrosis are found around the hepatic veins. In the centre of the necrotic areas a yellow pigment resembling hæmosiderin is present in abundance. The spleen is invariably enlarged, and also contains necrotic areas with pigment in the pulp, but the Malpighian bodies themselves are not affected. The lymphatic glands contain large macrophage endothelial cells infested with rod-shaped bodies. The lesions in the viscera are considered by Strong to be due to toxins liberated by the parasite. The bone-marrow shows proliferation, necrosis, and marked phagocytosis of the large endothelial cells.

Symptoms.—The incubation period of Oroya fever is about three weeks; its onset is insidious and is marked by malaise, soon followed by a rapidly developing pernicious anæmia and an irregular pyrexia associated with very severe pains in the head, joints, and long bones. The bone pains are probably associated with the disturbances in the hæmatopoietic system. Very often the initial fever is like that of a malaria infection, and may be the outcome of a double infection in a malarial subject. The

Digitized by Google

liver and spleen are enlarged and tender. The anæmia develops with great rapidity; and the death-rate varies from 10 to 40 per cent. of those attacked, the end coming within two or three weeks of the onset of the disease. A terminal delirium is often noted.

Treatment.—So far, no specific treatment has been devised, though it is said that salvarsan in doses of 0·2 grm. given by the intravenous route has a beneficial effect.

Prophylaxis.—Where possible, workmen in endemic districts should quit the locality before sunset. On a certain railway running through the endemic zone, where the mortality from this disease was enormous, by Dr. Giana's advice the workmen were obliged to quit the locality before sunset; the case-incidence immediately diminished.

Verruga Peruviana

Definition.—A remarkable granulomatous eruption, of unknown etiology, confined to certain parts of Peru, of extreme chronicity, and associated with hæmorrhages, fever, and joint pains.

Geographical distribution.—As in the case of Oroya fever, verruga appears to be confined to the borders of Peru, more especially to the Andes. Its range is coextensive, as far as one can judge at present, with that of the former disease.

Etiology.—Superficially, the lesions of verruga resemble those of yaws, and it has been suggested that it is merely a form of that disease modified by some local circumstance, such as altitude. No spironemata have been found in the lesions, and the Wassermann reaction is negative. Strong and the Harvard Commission found that they could communicate the disease from one man to another, as well as to monkeys, by rubbing into the eyebrow the material obtained from a verruga granuloma.

Rabbits and dogs may be infected either by the intratesticular or intraperitoneal route by injection of triturated granulomatous tissue. Certain chlamydozoa-like bodies have been found in the granulomatous tissue by da Rocha Lima, and it would appear from Strong's work that the unknown virus is too large to pass through a filter and that the filtrate is non-effective. It is suggested that there is an analogy between the virus of verruga and that of smallpox. More recently Strong has shown that there occurs a cloudiness of the medium, and an accumulation of a precipitate at the sides of the tube, when portions of the warts are removed with aseptic precautions and inoculated into serum according to Noguchi's method.

Digitized by Google

The granulomatous tissue contains a very active hæmolysin.

Strong's experiments upon monkeys showed that by graduated inoculation he was able to induce an artificial immunity in these animals. He therefore hopes to elaborate a suitable vaccine for man by employing a virus attenuated by frequent passage through appropriate animals.

From the fact that verruga is so readily conveyed by inoculation it has been argued that the infection is carried by night-feeding insects.

Pathology.—The pathological changes are very similar to those found in yaws. Primarily they consist of a proliferation of the endothelium of the lymphatic channels, which become obstructed by plasma cells and fibroblasts. The capillary blood-vessels become dilated, so that the granulomatous tumours are vascular, almost cavernous, and prone to bleed profusely. A feature of the pathological histology is the formation round the blood-vessels of nodules or angioblasts characteristic of the disease.

Symptoms.—The period of incubation, as shown by animal inoculation, varies from ten to forty-five days. The initial stages are characterized by peculiar rheumatic-like pains and initial fever, the pains being apparently the same in character as those of yaws, only more severe, and, as in yaws, the constitutional symptoms subside on the appearance of the skin lesion. The eruption, like that of yaws, may be sparse or abundant, discrete or confluent. As in yaws, individual granulomata may fail to erupt; others may subside rapidly; yet others may continue to increase, and then, after remaining stationary for a time, gradually wither, shrink, and drop off without leaving a scar. If difference there be in their clinical features between verruga and yaws, apparently it is more one of degree than of kind.

The eruption is generally described as being of two types, miliary and nodular, the former not exceeding the size of a small pea, the latter the rarer form of the two, less numerous, but consisting of much larger nodular masses. The miliary eruption, as a rule, is found most abundantly on the face and extensor aspect of the extremities, less commonly on the trunk.

A pink macule first appears, which later darkens in colour and becomes nodular. These nodules may be flat or somewhat pedunculated.

In yaws we find no mention made of the occurrence of fungating granulomata in any situation but the skin. In verruga it would seem that these vascular lesions may develop on mucous

Digitized by Google

surfaces—in the œsophagus, the stomach, intestine, bladder, uterus, and vagina. (Fig. 114.) Hence the dysphagia—a common symptom—and the occasional occurrence of hæmatemesis, melæna, hæmaturia, and bleeding from the vagina in this disease. Relapses both of the fever and of the eruption may occur.

The tendency to spontaneous hæmorrhage is attributed to the diminished atmospheric pressure at high altitudes, for it is said that when patients descend to the lower valleys or the sea-level the proneness to bleeding ceases.

The nodular eruption is more chronic than the miliary; in-

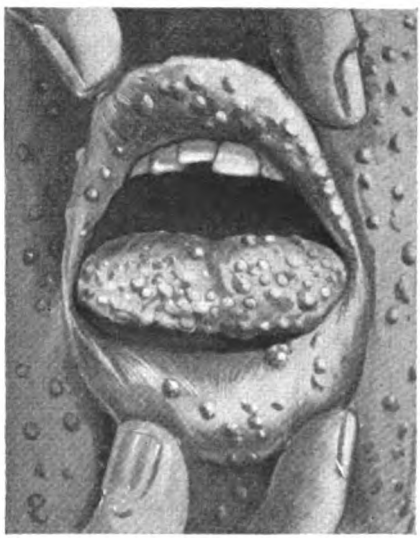


Fig. 114.—Verruga peruviana: showing nodules on skin and on mucous membrane of mouth. (*After Biffi.*)

dividual lesions may grow to the size of a pigeon's egg; they may become strangulated and a source of danger from hæmorrhage. This type of eruption does not invade the mucous membranes, and is usually confined to the regions of the knees or elbows. It appears in crops, and the duration of the disease extends over two or three months.

Diagnosis.—The appearances of verruga are so characteristic that it is hardly likely to be mistaken for any other disease. Conceivably it may closely resemble the frambœsiform eruption of secondary yaws; it may also be simulated by multiple warts, molluscum fibrosum, multiple fatty tumours (Dercum's disease),

Digitized by Google

and, according to Strong, it is closely allied to, if not identical with, Bassewitz's angio-fibroma cutis conscriptum contagiosum. Individual tumours may resemble a fibro-sarcoma or an angioma.

Treatment.—Very little appears to be known about the treatment of this condition. Small doses of salvarsan, 0·2 grm. intravenously, have been tried with benefit. When individual tumours begin to ulcerate or become gangrenous they should be excised. Dangerous bleeding may occur, and styptics or compresses may be required to stay the excessive loss of blood.

Digitized by Google

CHAPTER XXXIX

ULCERATING GRANULOMA OF THE PUDENDA

Synonyms.—Granuloma Venereum; Granuloma Inguinale.

Definition.—An infective and granulomatous condition of the pudenda, widespread in some parts of the tropics, conveyed by sexual contact and auto-inoculation.

Geographical distribution.—Ulcerating granuloma, or the "serpiginous ulceration of the genitals" referred to by Macleod and Maitland, is widely diffused in India, Guiana, Brazil, Papua, and northern Australia, and sporadically in the southern United States, the West Coast of Africa, and southern China.

Etiology.—Various spirochætes and micro-organisms have been described in this condition, though their specificity has been by no means established.

There is reason for believing that the disease is generally, though not invariably, a venereal one. Maitland has seen it in the mouths of a husband and wife. He considers that it may be inoculated on other forms of venereal sore, such as ulcerating bubo, and that thus a compound sore may result.

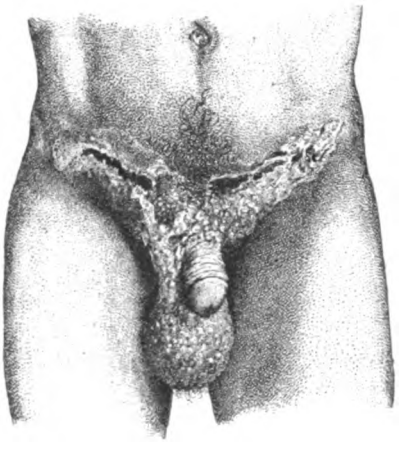
Donovan and Carter in India, Cleland and Strangman in Australia, Flu in Surinam, and Aragao in Brazil, have described certain parasitic bodies within the large mononuclear cells from scrapings of these lesions. The organism is like a short bacillus with rounded ends, and measures 1 μ by 0·2 μ. De Souza Araujo, in 1912, named it *Calymmato-bacterium granulomatis*. It was re-studied in 1917 by E. L. Walker, who finds the organism to be a capsulated intracellular diplococcus, probably *Bacillus mucosus capsulatus*, one of the Friedländer group. It is easily cultivated on Sabouraud's medium after forty-eight hours' incubation, though it appears to thrive as well on other laboratory media. In the sores it is found in the deeper layers of the tissues. Cultures of the organism are pathogenic to mice and cause subcutaneous abscesses when injected into these animals; in rabbits it produces elevated nodules. There are reasons for believing that this organism represents merely a secondary infection, and that the main cause of ulcerating granuloma remains to be discovered.

Age and sex.—Ulcerating granuloma has not been observed

Digitized by Google

before puberty; it has been found only after the age of 13 or 14, and up to 40 or 50. It occurs in both sexes, but more often in women, especially where polyandry is practised.

Symptoms.—The disease commences in the great majority of cases somewhere on the genitals, usually on the penis or labia minora, or on the groin, as an insignificant, circumscribed, nodular thickening and elevation of the skin. The affected area, which on the whole is elevated above the surrounding healthy skin, and covered with a very delicate, pinkish, easily-rubbed-off epithelium, excoriates readily, exposing a surface prone to bleed and break down, although rarely ulcerating deeply. The disease



TERZI.—

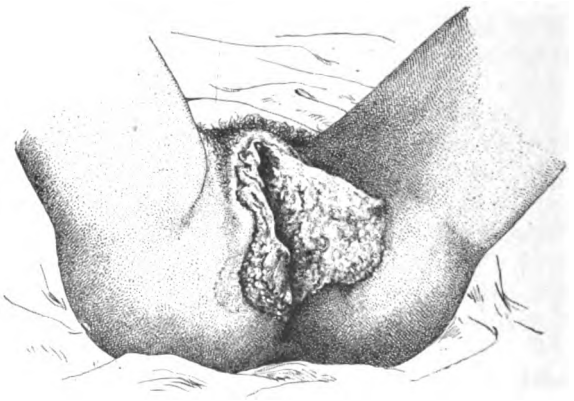
Fig. 115.—Ulcerating granuloma of pudenda in the male.

advances in two ways: by continuous eccentric-peripheral extension, and by auto-infection of an opposing surface. In its extension it exhibits a predilection for warm and moist surfaces, particularly the folds between the scrotum and thighs, the labia, and the flexures of the thighs (Fig. 115). Its extension is very slow, years elapsing before it covers a large area. Concurrently with peripheral extension a dense, contracting, uneven, readily-breaking-down scar forms on the surface travelled over by the coarsely or finely nodulated elevated new growth which constitutes the peripheral part of the diseased area. Occasionally islands of active disease spring up in this scar tissue; but it is at the margin of the implicated patch that the special features of the

Digitized by Google

affection are best observed. In a case of some standing there is found a large area of white or irregularly pigmented, perhaps excoriated, unsound, contracting, folded, and dense cicatrix surrounded by a narrow, serpiginous, irregular border of nodulated, somewhat raised, red, glazed, delicately skinned or pinkish, superficially ulcerated or cracked new growth. Occasionally the glans penis is not involved.

In the case of the female (Fig. 116) the disease primarily attacks the crura of the clitoris, thence extending into the vagina, over the labia, and along the flexures of the thighs. The women thus affected are rendered sterile; the lymphatic glands are said to be enlarged in the neighbourhood of the lesions. In the male



TERZI.

Fig. 116.—Ulcerating granuloma of pudenda in the female.

the disease may spread over the penis, involve the glans, scrotum, and upper part of the thighs. In either sex it may spread in the course of years to the pubes, over the perineum, and into the rectum, the recto-vaginal septum in the female ultimately breaking down. At times a profuse watery discharge exudes and even drips from the surface of the new growth, soiling the clothes, soddening the skin, and emitting a peculiarly offensive odour. In this condition the disease, slowly extending, continues for years, giving rise to inconvenience, and perhaps seriously implicating the urethra, vagina, or anus, but not otherwise materially impairing the health. In male patients the lymphatic glands do not become affected. The disease continues entirely local.

Histology.—Histologically this disease is allied to rhinoscleroma. On microscopical examination the new growth at

Digitized by Google

the margins of the sore is found to be made up of nodules, or masses of nodules, consisting of round cells having large and, usually, badly staining nuclei. These cells are embedded in a delicate fibrous reticulum. The nodular masses are, for the most part, covered by epithelium, their under surfaces merging gradually into a thick, dense, fibrous stroma in which small clusters of similar round cells are here and there embedded. The growths, though very vascular, contain no hæmorrhages; and there are no signs of suppuration or of caseation, no giant cells, and no tubercle bacilli. In vertical section of the small nodules the round-cell mass will be found to be wedge-shaped, the base of the wedge being towards the surface; the deep-lying apex is usually pierced by a hair or two. The growth is found around sebaceous follicles, blood-vessels, lymphatics, and sudoriparous glands; but it is especially abundant, and most deeply situated, around the hair-follicles.

Diagnosis.—Malignant and syphilitic ulcerations of the groin are common enough; the disease under notice, however, differs widely from these—clinically, histologically, and therapeutically. It is characterized by extreme chronicity—ten or more years; by absence of cachexia or of any tendency to cause death; by non-implication of the lymphatic system, and by non-amenability to mercury and iodide of potassium. The disease which it most resembles is lupus vulgaris. From this it differs inasmuch as it is practically confined to the pudendal region; tends to follow in its extension the folds of the skin; is not associated with the tubercle bacillus, giant cells, caseation, or other evidences of tuberculous disease.

Treatment.—Scraping and caustics, including the actual cautery, have been freely employed; but, although some improvement may be effected by these means, new nodules almost invariably spring up in the resulting cicatrix. Until recently complete excision, where practicable, offered the best chance of permanent cure; such a proceeding had to be undertaken before large areas and important passages had become involved.

Judging from its relatively superficial nature and close resemblance to lupus, it seemed probable that ulcerating granuloma might prove amenable to some form of radiotherapy. This is actually the case, and X-rays, originally suggested by Sequeira and Macleod, are now regularly and successfully employed in Madras in the treatment of the disease. Of 37 cases treated in this way in Madras Hospital in 1908, all proved successful within an average period of two months. In three of the cases which

Digitized by Google

could be followed up there was no recurrence four months after their discharge.

Treatment by intravenous injections of tartar emetic, introduced by Aragao and Vianna in 1913, has proved also remarkably successful. Improvement usually sets in, and, although in a small proportion of cases relapse occurs, in the vast majority the cure is radical. The initial dose should be 5 c.c. of 1-per-cent. solution in normal saline, cautiously increased to 10 or 12 c.c. given daily or every second day. At the same time the sore should be dressed twice daily with compresses soaked in a 1-per-cent. solution, diluted if necessary. The surface of the sore may be dusted with antimony oxide, zinc oxide, and calomel in equal parts. The tartar emetic solution may be combined with or supplemented by the X-rays.

It may be necessary to give large amounts of antimony tartrate ; according to Low 50 gr. or more may be required.

Certain cases, such as one recently reported by Low and Newham, may be refractory to any form of treatment.

Digitized by Google

Section V.—ANIMAL PARASITES AND ASSOCIATED DISEASES

CHAPTER XL

PARASITES OF THE CIRCULATORY SYSTEM

SCHISTOSOMIASIS

Definition.—A group of diseases caused by certain digenetic trematodes of the order Schistosomatidæ which inhabit the venous system of man in various tropical and subtropical countries.

I.—URINARY SCHISTOSOMIASIS

Schistosoma hæmatobium (Bilharz, and v. Siebold, 1852)

Synonyms.—Bilharziasis; Bilharzia Disease; Endemic Hæmaturia.

Definition.—A chronic endemic disease produced by infestation of the pelvic veins, particularly those of the bladder and, occasionally, those of the rectum, by *Schistosoma hæmatobium* (*Bilharzia hæmatobia*, *Distomum hæmatobium*), the eggs of which, being deposited in the mucous membrane of the bladder, give rise to hæmaturia and cystitis or other symptoms connected with the urinary organs and, occasionally, when deposited in the rectum, to muco-sanguineous discharges from the bowel. In the earlier stages toxæmic symptoms have been noted. The eggs of the parasite are discharged in the urine and, in certain cases, in the fæces.

History and geographical distribution.—The frequency of hæmaturia in the natives of Egypt and in visitors to that country has been known since the earliest times. The explanation was supplied by Bilharz, who, in 1851, discovered the cause in a peculiar digenetic trematode which, in 1859, Cobbold proposed to name *Bilharzia* in honour of its discoverer. As Weinland had previously given the name *Schistosoma* to the genus, this is now generally accepted by zoologists as the proper generic term.

In 1864 Dr. John Harley recognized the characteristic ova in cases of hæmaturia from Natal. The disease has since been found in many other parts of Africa, more particularly along the

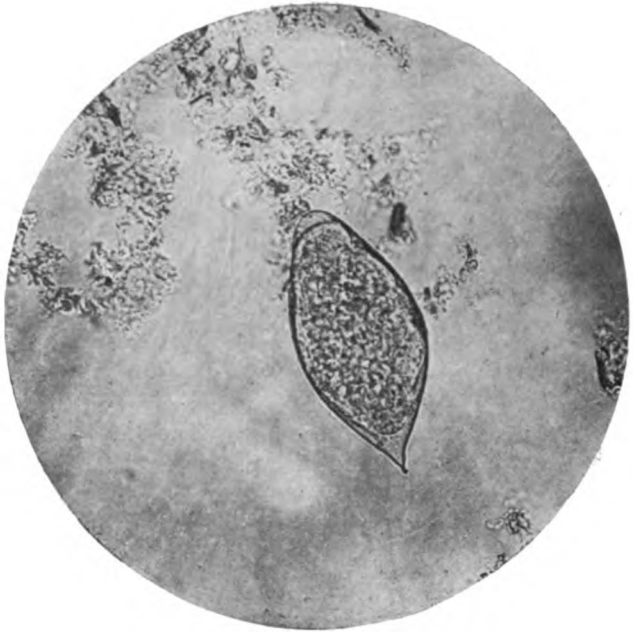
Digitized by Google

eastern side of the continent as far south as Port Elizabeth. In Central Africa it occurs in the Sudan, Uganda, and Rhodesia, and it is met with in West Africa as well. In North Africa it is especially common in Morocco, Algiers, Tunis, and Egypt. It also occurs in Arabia, parts of Palestine near Jaffa, Persia, Mesopotamia, Cyprus, Mauritius, Réunion, and Madagascar. It is doubtful whether the indigenous cases of the urinary form of this disease reported from Central and North America, the West Indies, and even from the British Isles are authentic. In Egypt, judging from Bilharz's, Griesinger's, and Sonsino's post-mortem records, it is present in quite one-half of the population; in one village, Marg, Leiper found that no fewer than 90 per cent. of the children were infected, and we have proof from the researches of Sir A. Rüffer that it was rampant many thousands of years before the Christian era. Indigenous infestation with this trematode has been reported from Western Australia, so that its extension in that continent is a possibility to be reckoned with.

The parasite.—*Schistosoma hæmatobium* (Figs. 117, 118, 119) is a bisexual trematode belonging to the family Schistosomidæ. The *male* is white, cylindroid, 11 to 15 mm. in length by 1 mm. in breadth. It possesses an oral and a ventral sucker (of which the latter is the larger), placed close together. The oral sucker has the dorsal lip longer than the ventral. The cylindrical appearance of the worm is produced by the ventral infolding of the two sides of what would otherwise be a flat body. By this infolding a gynæcophoric canal is formed, in which the female can be partially enclosed. The outer surface of the body is closely beset with small cuticular prominences, especially on the dorsal surface. There are delicate spines on the suckers, and the largest tuberculations are situated on the inner surface of the gynæcophoric canal. The *female* is rather darker in colour than the male, considerably longer (20 mm. by 0·25 mm. in breadth), more filiform, her middle portion being usually infolded in the gynæcophoric canal of the male, whilst her anterior and posterior portions remain free. Her body is smooth except towards the posterior end and on the suckers, where papillæ abound. The genital openings of the sexes face each other, and are placed immediately posterior to the ventral sucker. The sexes live apart while young, but on reaching maturity the female enters the gynæcophoric canal of the male. The alimentary canal commences at the oral sucker; the ventral sucker, or acetabulum, being prehensile in function. The œsophagus presents two dilatations, and bifurcates just in front of the acetabulum to form two intestinal tubes, which again unite into a median trunk. The excretory system consists of two longitudinal canals which open posteriorly and somewhat dorsally by the excretory pore.

These parasites are found in the blood of the portal vein, in its mesenteric branches, but occur in greatest numbers in the pubic plexuses, the vesical and uterine; hence worms may wander into the vena cava, and may be actually filtered out in the lungs. Their numbers vary considerably; as many as 300 may be found in the portal vein and its branches; in experimentally infested monkeys they may be even more numerous. Looss has

Digitized by Google



Terminal-spined egg of Schistosoma hæmatobium.

(*Microphoto: Dr. Bell.*)

Lateral-spined egg of Schistosoma mansoni.

(*Microphoto: Dr. Kerr.*)

SCHISTOSOMA EGGS. × 250.

PLATE XXI.

Digitized by Google

Digitized by Google

seen the submucous tissue of the bladder so rich in worms that a pair could be found in every area of half a centimetre square.

The ovum.—On microscopical examination the uterus of the female worm is found to be stuffed with ova of a peculiar and characteristic shape. They are oval, each egg on an average measuring about 0·16 mm. in length by 0·06 mm. in breadth. One end of the ovum is provided with a short, stout, and very definite spine. (Plate XXI., Fig. 1.)

The exact nature of the process by which the ova leave the body of the human host has been explained by Fairley and the Editor from observations

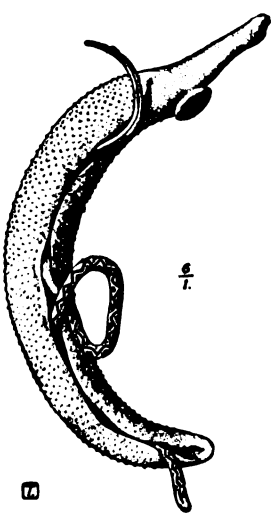


Fig. 117. — Schistosoma hæmatobium, male and female. (*Partly after Looss.*)

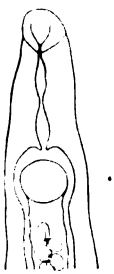


Fig. 118.— Schistosoma hæmatobium: anterior end of male. (*After Looss.*)

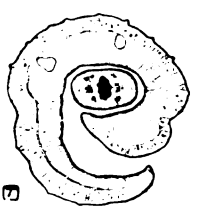


Fig. 119.— Schistosoma hæmatobium. Diagram of transverse section of male and female.

upon experimentally infested monkeys whose mesentery had been exposed under anæsthesia. The paired worms travel against the bloodstream to the furthermost possible point, where the female leaves her partner, and, being of a smaller diameter, is able by means of her suckers to progress until she stretches the smaller venules to their uttermost. The ova are now deposited with their spines directed posteriorly in front of the anterior sucker. The female then withdraws a little and repeats the process. On the resumption of the blood current the vessel wall contracts upon the contained ova and drives the spine through the vessel wall. It would appear that ova, but freshly deposited in this manner in the submucosa of the bladder, are voided in the urine only a few hours subsequently, and it is due to the rupture of

Digitized by Google

these small blood-vessels that the blood leaks out into the urine at the same time. (Fig. 120.)

In a large proportion of cases, much more frequently than was formerly thought to be the case, the characteristic ova of *S. hæmatobium* may be found in the fæces (Fairley), though it has not yet been proved that they are capable of forming the intestinal papillomata so characteristic of *S. mansoni* infestations.

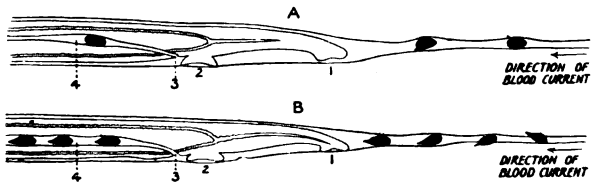


Fig. 120.—Diagram representing deposition of ova by (A) S. mansoni, and (B) S. hæmatobium in blood-vessels, and their passage to exterior. (*Orig.*)

1, Anterior sucker; 2, posterior sucker; 3, vaginal orifice; 4, uterus with contained ova.

The free embryo (Fig. 121).—In newly voided urine the ovum presents a somewhat brownish appearance, and generally contains a ciliated embryo (*miracidium*). After a time the embryo may escape through a transverse rupture in the shell, which is produced by the absorption of water. It then swims about, but, unless supplied with fresh water, soon perishes. If the urine be freely diluted with water the embryo not only escapes more quickly from the shell, but also continues to live, swimming and gyrating very actively, for a maximum of thirty-six hours. While swimming, the body of the little animal undergoes many changes of shape. For the most part, when advancing, it is oblong, tapering somewhat posteriorly; when more stationary it tends to assume a spherical form. It moves by means of the cilia which, with the exception of the minute papillary beak, thickly cover the entire body. On careful examination, a primitive intestine may be traced from the anterior papilla; on each side of this, two unicellular salivary, or cephalic, glands can be made out, with ducts opening into the mouth. The bulk of the embryo is occupied by a number of germ cells, the posterior part by excretory tubules connected with four large flame-cells. The nervous system is represented by an oval, irregular mass lying in the centre of the body. According to Leiper and Ashworth's observations the cuticle of the miracidium is composed of a number of polygonal epithelial cells. The body is divided transversely into three zones, united by six or seven longitudinal strands.

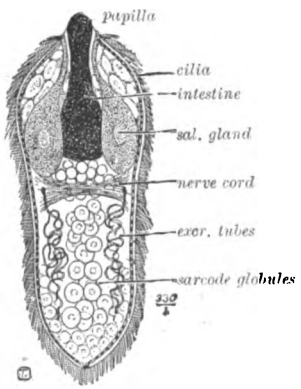


Fig. 121.—Schistosoma hæmatobium miracidium. (*After Looss.*)

Digitized by Google

Life-history.—Beyond its first stage of free-swimming ciliated embryo, the extracorporeal life of *Schistosoma hæmatobium* was until quite recently unknown. Leiper's remarkable work in Egypt, however, has completely filled in this hiatus in our knowledge of the life-history of this important parasite. It is therefore no longer necessary to describe, as in former editions of this manual, the many attempts that had been made previously to trace the progress of the miracidium. Leiper showed (1916) that the miracidia of *S. hæmatobium* and of *S. mansoni*, after escape from the egg, enter a fresh-water snail; in the case of *S. hæmatobium*, a bullinus (*B. dybowski, B. innesi, B. contortus*) (Fig. 122, 1, 2, 3; in the case of *S. mansoni, Planorbis boissyi* (Fig. 129)—small molluscs abounding in the

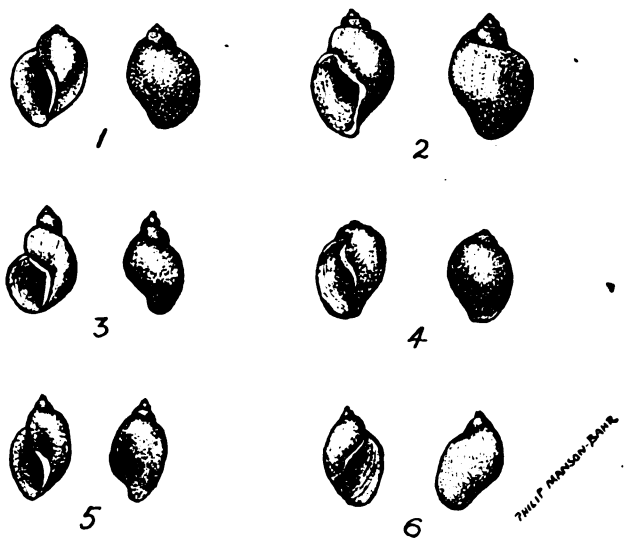


Fig. 122.—Fresh-water molluscs. Nat. size. (*Orig.*)

1, Bullinus contortus; 2, B. dybowski; 3, B. innesi; 4, Physopsis africanæ—all intermediary hosts of S. hæmatobium; 5, Physa subopaca, a sinistral snail apt to be mistaken for Bullinus; 6, Limnæa laurenti, a dextral snail.

irrigation canals of Egypt. According to Lutz, the miracidia, after penetrating the antennæ of the mollusc, cast their cilia and become converted into a sporocyst, in the interior of which daughter sporocysts form. These latter migrate to the liver and hermaphrodite gland, where they multiply by transverse fission (Fig. 123) to such an extent that the entire liver becomes permeated with the long, delicate, transparent tube-like bodies. Presently numberless bifid-tailed cercariæ develop within the sporocysts (Fig. 124), and on maturing escape spontaneously into the surrounding water. Opportunity occurring, the now free cercariæ penetrate the skin of some suitable vertebrate—man, mouse, rat, monkey—dropping their tails in the passage. Entering lymphatics or blood-vessels, they proceed to the liver of the definitive host, and in the course of about six weeks attain sexual maturity and produce terminal or lateral-spined eggs according to species. To obtain

Digitized by Google

these results in the laboratory, all that is necessary is to place the living experimental animal, or a part—tail, limb, etc.—of such animal, in the water into which cercariæ have escaped from the snail, care being taken that the dose of cercariæ is not too large, as in such case the excessive invasion of the liver may prove rapidly fatal. The experimenter should be very careful to avoid bringing cercariæ-containing water into contact with his own skin. As molluscs are liable to invasion by a variety of miracidia, sporocysts, and cercariæ of many species of trematodes, it is necessary for those who would confirm Leiper's discoveries that they should be able to recognize the specific features of the cercariæ of *S. hæmatobium* and *S. mansoni*. Leiper lays stress on four points, viz. that (1) these cercariæ have no pharynx; (2) they have forked tails; (3) they have no "eyespots," that is, two minute collections of dark pigment located in the anterior third of the body on either side of the middle line between the suckers—a feature of certain other fork-tailed

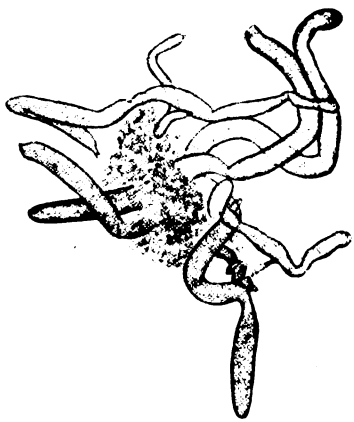


Fig. 123.—Schistosome daughter-sporocysts teased from liver. (*Leiper.*)

cercariæ, but absent in schistosoma; (4) they have two sets of glands communicating with the mouth, and lying on both sides of the posterior end of the body. The excretory system consists of six flame-shaped cells in the body and two in the anterior region of the tail. The cuticle of all fork-tailed cercariæ is beset with minute spines. Leiper has shown further, to use his own words, "that those animals infected with cercariæ from *Bullinus dybowski*, etc., always produce adult worms which give rise to terminal-spined eggs only, while those infected with cercariæ from *Planorbis boissyi* give rise equally constantly to lateral-spined eggs. In no case do both varieties arise from the same intermediate host. Moreover, the adult worms reared from these two sources show constant..... morphological differences." In the adult *S. hæmatobium*, reared from cercariæ developing in *Bullinus*, there are four or five large testes, and the gut branches do not unite until late, resulting in a short cæcum. In the adult *S. mansoni*, reared from cercariæ developing in *Planorbis boissyi*, there are eight or nine testes, and the gut branches unite early, forming a long cæcum. In the female *S. hæmatobium* the uterus contains many eggs, and the ovary is situated in the posterior half; whereas in *S. mansoni* it is short and contains only one or

Digitized by Google

two eggs, and the ovary lies in the anterior half of the body, in front of the union of the gut. *S. mansoni*, unlike *S. hæmatobium*, always causes a heavy deposition of black granules in the liver of the human host. Lastly, as

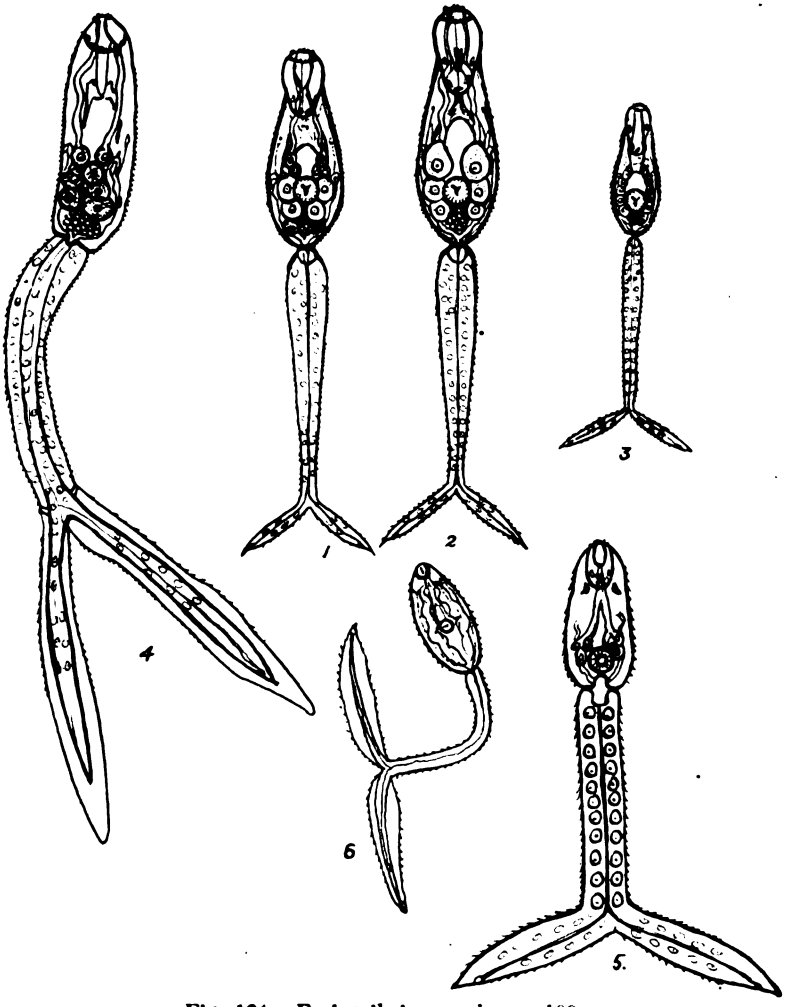


Fig. 124.—Fork-tailed cercariæ. × 100.

(Partly original, partly after Leiper, Faust, and Looss)

1, S. mansoni cercaria; 2, S. hæmatobium cercaria; 3, S. japonicum cercaria; 4, Cercaria gladii; 5, C. minor; 6, C. vivax.

regards habitat: the males of *S. hæmatobium* appear to leave the liver early and to pass down into the finer branches of the mesenteric veins before they attain maturity, while the females found in the gynæcophoric canal are

Digitized by Google

diminutive; the males of *S. mansoni* remain in the liver until the females *in copula* begin to lay eggs, and large numbers of lateral-spined eggs are frequently deposited in branches of the portal system. (Figs. 285, 286.)

Lutz has found that *Planorbis olivaceus* is the intermediary host of *S. mansoni* in Brazil, and Becker in South Africa has confirmed Leiper's work * as regards *S. hæmatobium*, the efficient species of host in that country being *Physopsis africana*, a mollusc closely allied to *Bullinus*. (Fig. 122, 4.)

Symptoms.—The symptoms produced by *S. hæmatobium* vary in degree within very wide limits. In the vast majority of instances the patient experiences no trouble whatever; in other instances the suffering is very great. Indirectly, from the serious nature of the lesions of the urinary organs to which it may give rise, the schistosoma is an occasional cause of death.

Early toxic symptoms, as in *S. mansoni* and *S. japonicum* infestations, have been noted, and may come on four weeks after exposure to infection. The incubation period of definite organic disease, on the other hand, varies within wide limits from three months up to two and a half years.

The most characteristic symptom of the presence of the parasite in the wall of the bladder is the passage of blood at the end of micturition, with or without a sense of urinary irritation. The quantity of blood passed and the degree of irritation are increased by exercise, by dietetic indiscretions, and by all such causes as are calculated to induce or aggravate cystitis. As a rule, it is only the last few drops of urine that contain blood; sometimes, however, the hæmorrhage is more extensive, and then the entire bulk of the urine may be blood-tinged. Occasionally, clots are passed.

If, in a case of moderate infection, the urine be passed into a glass and held up to the light, minute flocculi or coiled-up mucoid-looking threads will be seen floating about in the fluid. If it be allowed to stand, the flocculi, and perhaps minute blood-clots, will subside to the bottom of the vessel; these, on being taken up with a pipette and placed under the microscope, will be found to contain, besides blood-corpuscles and catarrhal products, large numbers of the characteristic spined ova.

In doubtful cases, where ova are few, the best way to find them is to get the patient to empty the bladder and to catch in a watch-glass the last few drops of urine which can be forced

* According to Leiper, more detailed work is necessary before the development of *S. hæmatobium* in the South African snails can be finally settled. *S. boris* also occurs in South Africa, and it now appears that the cercariæ described by Cawston as those of *S. hæmatobium* may belong to this species. A. Porter has recently stated that fork-tailed cercariæ presumed to be of *S. hæmatobium* have been found in Natal in *Limnæa natalensis*.

Digitized by Google

out by straining; these invariably contain ova. A low power of the microscope suffices, and is best for diagnosis.

Pain is by no means always a dominating feature; when it occurs it generally assumes the form of a dull sense of oppression in the suprapubic region, deep-seated perineal pain, or scalding on micturition. Frequency of micturition is an early, and urgency a very common, symptom. Rectal symptoms, with passage of blood and mucus, may coexist with the urinary symptoms, and a digital examination may detect ulceration above the prostatic lobes. This localized lesion may be due to *S. hæmatobium* alone, though it must be remembered that mixed infestations of both trematodes (*S. hæmatobium* and *S. mansoni*) are very common, especially in the Nile Valley. Sometimes adult worms *in copula* are passed in the urine; generally after a copious hæmorrhage due to a ruptured vessel.

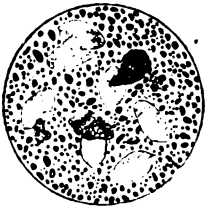


Fig. 125.—Section through nucleus of urinary calculus containing ova of Schistosoma hæmatobium.

Endemic hæmaturia lasts for months or years. Spontaneous recovery is rarely complete. In ordinary cases, provided no reinfection take place, the hæmaturia tends to decrease, although ova may continue for years to be found in the last few drops of urine passed. In severe cases, sooner or later, signs of cystitis supervene and give rise to a great deal of suffering. Not infrequently the ova become the nuclei for stone, and symptoms of urinary calculus are superadded. (Fig. 125.) Sometimes the pathological changes induced by the presence of the parasite in the bladder lead to the development of new growth, in which event the symptoms become more urgent and the hæmaturia perhaps excessive. Hypertrophy, contraction, and even dilatation of the bladder are not unusual. Besides the bladder symptoms there may be signs of prostatic disease, or of disease of the vesiculæ seminales causing spermatorrhœa. In the latter case, ova may be detected in the semen. In other instances the ureters and kidneys become involved, resulting in ureteric dilatation and hydronephrosis. Secondary septic infection of the urinary tract with septic cystitis commonly supervenes. In consequence of the suffering which these aggravated forms of infection produce, the patients become anæmic, wasted, debilitated, and a ready prey to intercurrent disease.

Milton has pointed out the extreme frequency of urinary

Digitized by Google

fistula in Egypt, the result of schistosome disease of the urethra. These fistulæ may occur anywhere in the neighbourhood of the genitals, but are especially common in the perineum and posterior surface of the scrotum, and originate from infiltration by ova of the pubic tissue or roof of the urethra just in front of the bulb, the eggs of the parasite being deposited in the mucous or submucous tissue. Stricture of the urethra is by no means uncommon from a similar cause, especially in the case of fistulæ connected with the floor of the urethra. In the male, infiltration of the penile sheath may result in an elephantoid condition with chordee and actual obstruction to the urinary flow. (Fig. 126.)

Fig. 126.—Urinary schistosomiasis; pseudo-elephantiasis of penis, due to infiltration by ova. (*After Madden.*)

Ferguson has pointed out the liability of bilharzial tumours to develop malignant changes.

Vaginitis and cervicitis have been known to be produced by this parasite. On the vulva papillomatous masses containing schistosome ova are, according to Madden, very common. We have seen similar excrescences about the anus and in the groin and perineum.

Large numbers of ova, as pointed out by Turner, may be deposited in the lungs, where they give rise to a form of interstitial pneumonia. They have been found also in the brain and spinal cord, thus accounting for epileptic and paralytic symptoms from which the patients had suffered during life; such symptoms supervene only in hyperinfected individuals.

Pathological anatomy.—The character of the changes brought about by the schistosoma varies very much according to the degree and the duration of the infection. In almost every case the walls of the urinary bladder are early affected. All that may be apparent to the naked eye at this stage is a certain amount of injection of the small vessels of the mucosa vesicæ, and certain exceedingly minute vesicular or papular elevations of the surface of this membrane. When these minute elevations are examined microscopically they are found to contain ova even in the minute blood-vessels. Later, especially in the trigone of the bladder, there are found rounded patches of in

Digitized by Google

flammatory thickening which project somewhat, are granular on the surface, and dense in consistence; on section they creak under the knife as if they contained gritty particles. It is evident that these elevated, thickened patches are the result of an inflammatory process provoked by the clusters of ova which the microscope reveals scattered throughout their entire extent. The ova are principally deposited in the submucosa, less extensively in the mucous membrane itself, still less abundantly in the muscular walls of the organ or in its subserous connective tissue. They

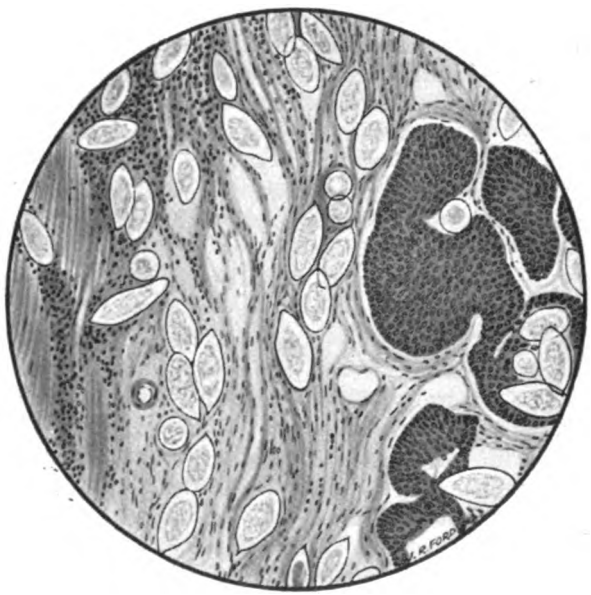


Fig. 127. – Section of bladder-wall, showing ova of S. hæmatobium in tissues.

tend to occur in groups, each of which is invested with a sort of connective-tissue capsule; or they may be lying in small blood-vessels which they occlude. Some ova are seen to have undergone calcification; others are still fresh, either segmenting, or already containing a miracidium. On the surface of the rounded patches already mentioned phosphatic deposits, also containing ova, are not uncommon; sometimes the patches present minute sloughs. (Fig. 127.) Besides these indurated patches, various forms of polypoid excrescence—sometimes ulcerated—may protrude from the mucous surface into the cavity of the bladder. These various hyperplasiæ frequently contain the adult parasite as well as ova.

Digitized by Google

In addition to what may be designated the specific changes in the mucosa, the muscular coats of the bladder are generally hypertrophied. In consequence of this, as well as of the ingrowth of villosities and different forms of new growth, the capacity of the organ may be much diminished. Its mucous surface is generally coated with a sanguineous mucus containing myriads of ova. Gravel or small stones—generally phosphatic—are sometimes found either embedded in lacunæ in the hypertrophied and roughened bladder wall or free in the cavity. Not infrequently a similar hyperplasia occurs in the ureters, and particularly towards their lower ends, even at an early stage of this disease. The urgency of early treatment in all cases of urinary bilharziasis is obvious. In rare instances the pelvis of the kidney itself is affected. Obliteration of the ureter, both from small stones and from thickening of the mucous membrane, has sometimes been met with; this leads to dilatation of the pelvis and atrophy of the parenchyma of the kidney. It is easy to understand how, in time, these changes in the bladder and ureters may give rise to hydronephrosis, pyelitis, abscess of the kidney, and similar secondary affections. Hyperplasia of the prostate due to infiltration with ova is sometimes found.

Hyperplasia from schistosoma infestation may also occur in the vesiculæ seminales, in the walls of the vagina, and in the cervix of the uterus, leading to corresponding bloody, ova-containing discharges.

It may be mentioned that schistosome ova in small numbers have been found in the liver, in gall-stones, in the heart, and in the kidneys. We have no knowledge of any definite pathological change entailed by their presence there. The occasional occurrence of ova in the brain, spinal cord, and lungs has already been noted. Tumours of schistosome origin have sometimes been found in connection with the peritoneum and ligaments of the uterus.

The ova can be conveniently demonstrated in the tissues by digesting selected portions in 3-per-cent. potash solution (Ferguson).

Diagnosis.—The diagnosis of this disease is not difficult; the presence of ova in the urine is decisive. In countries like Egypt, where the disease must often concur with chyluria, with stone, with vesical tumour, with gonorrhœal cystitis, and with pyelitis, as well as with prostatic disease, care must be exercised in each particular case to separate the special factors to which the various symptoms are attributable. Thus in chyluria concurring with schistosome disease there will be chyle in the urine

Digitized by Google

in addition to blood. In such a combination the clot which forms will be larger, will contain oil granules and globules, and very probably microfilariæ, in addition to schistosome ova; moreover, the microfilariæ will generally be detectable in the finger blood if looked for at night. Stone in the bladder, when suspected, has to be searched for with the sound. In gonorrhœal cystitis the history of gonorrhœa will be forthcoming. In prostatic disease enlargement of the prostate may be made out. Difficulty may sometimes arise when ova are few in number, or when they have ceased altogether to come away in consequence of the death of the parent worms. The mischief wrought by the parasite remains, although the ova—the most certain evidence of the parasite's previous presence—may be discharged no longer. But, even if ova are very few, they may still be found in the last drop or two of urine passed. If they are no longer to be found in the urine, sometimes, by scratching the surface of the bladder with a sound and examining the shreds of mucus so obtained, a few, calcified it may be, but presenting the characteristic spine, may be seen with the microscope.

Fairley's reaction.—Fairley in 1917 devised an ingenious complement-deviation reaction by employing as antigen an extract of the livers of infested snails (*Planorbis boissyi*). The antigen is prepared by macerating a number of livers containing cercariæ of *S. mansoni* in absolute alcohol, filtering, and evaporating by means of a Sprengel's pump. A saline extract is then made of the dried residue and the anticomplementary dose estimated. The general technique employed is the same as for the quantitative Wassermann reaction in syphilis.

The reaction is apparently a group one, in so far that an antigen prepared from cercariæ of *S. mansoni* will give positive results with *S. hæmatobium* serum, but it has been proved to be absolutely specific for both urinary and rectal bilharziasis and to occur in 89 per cent. of early cases of the disease. A positive result may be obtained in early infestations before the appearance of ova in the dejecta. It is not so specific in the later as in the earlier stages of the disease. This work was confirmed by W. A. Murray in South Africa (1920).

Cystoscopic examination.—In the early stages of the localized disease (within two months of infection) the cystoscope reveals sparse grey discrete elevations in the trigone around the ureteric orifices; later, definite hæmorrhagic papules appear with surrounding inflammation. Later still, characteristic "sandy patches" and papillomata can be distinguished.

Digitized by Google

Prognosis.—An important element to be considered in venturing on a prognosis is the long life of the parasite. The British Government is still paying pensions to the subjects of infestations contracted in South Africa more than nineteen years ago. Another important element in prognosis is the degree of infection; the greater the number of worms the more severe and the more extensive the disease they produce. As with filarial infection, the greater the number of cases in a district the greater the proportionate probability of severe infections being met with. The prognosis is practically that of a chronic cystitis depending on a remediable, and not in itself fatal, cause. Much suffering may often be produced, and, as a consequence, anæmia and debility. Possibly calculus may be formed; possibly grave renal disease may ensue; possibly villous or epitheliomatous growths in the bladder. In the milder degrees of infection, which fortunately are the commonest, the patient seems to be in no way inconvenienced by the parasite, and generally escapes all serious consequences. In any case, mild or severe, there may be attacks of hæmaturia from time to time; as a rule, the quantity of blood lost is insignificant.

Treatment.—The treatment of schistosome infestations was introduced and placed upon a sound basis by Christopherson in Khartum. By the intravenous injection of antimonium tartratum (*tartar emetic*) he reported the cure of the disease in 70 cases. His results have been confirmed by Taylor, Fairley, Low, Newham, Madden, and Day. The drug appears to act upon the adult worm by a cumulative action, and its results are controlled by observations upon the ova in the urine. For this purpose the freshly-passed urinary deposit is mingled daily with about sixty times the amount of warm tap-water at about 130° F., and the hatching of the ova is watched. Under normal conditions they are hatched in about five minutes; after the injection of antimony tartrate it is found that they are no longer passed, and that such ova as may appear in the urine are dark and shrivelled. It is thought that the appearance of the ova altered in this manner, or their absence, coincides with the death of the adult worm.

It should be noted that living ova left too long in contact with alkaline urine fail to hatch; therefore all experiments should be performed with freshly-voided urine.

The intravenous injections are given on alternate days over a period of fifteen to thirty days. Christopherson begins with ½ gr. of tartar emetic dissolved in 6 c.c. of sterile normal saline solution. The stock solution of tartar emetic is made up in a

Digitized by Google

sterilized vaccine bottle with a rubber cap, in a strength of ½ gr. to 1 c.c. of distilled water; for use this is diluted with 5 c.c. of sterile saline. The resulting solution is drawn into the barrel of a 10-c.c. syringe and slowly injected into a prominent vein, preferably the median basilic or cephalic. Care must be taken that none of the solution escapes into the surrounding tissues, as an abscess may result. The injection is repeated every other day and increased by ½ gr. up to a maximum of 2½ gr. at a single sitting. In giving the larger doses the total amount injected at a time is made up to 10 c.c. with sterile saline.

The total injected may amount to 20–30 gr. of tartar emetic. Further observations may prove that this amount is too large. A rapid improvement in the condition of the urine is soon observed; generally all traces of blood disappear after the injection of 15 gr.

If given slowly and in the manner indicated, but few untoward effects are noted. These generally consist of cough and pharyngeal irritation coming on while the drug is being administered; nausea and occasionally vomiting may supervene.

For children a total of 10 gr. appears to be sufficient. Recent experience shows that short cumulative courses are more efficacious than are more prolonged and interrupted ones.

It is advisable to make the patient lie down for a few hours after the injection. Until further researches have been made it is inadvisable to treat elderly patients or those with renal or cardiac disease by this method, though it is possible that less toxic combinations of antimony may be discovered. Rogers has already suggested the substitution of the ammonium for the potassium salt of antimony and the employment of colloidal antimony sulphide.

Recently *emetine* has been given with apparent success by Diamantis in Egypt. This intramuscular injection is advocated for those patients, especially children, who are intolerant of antimony or whose veins are too narrow for intravenous injection, but wherever possible it should be given by the venous route in a 3-per-cent. solution in sterilized water, the dose being 2 c.c., containing 1 gr. of the salt. The maximum single dose is 3 gr. for an adult. Generally one commences with ½-gr. doses. A total amount of 15–20 gr. may be given altogether.

Local applications are useful. Excessive catarrh of the bladder suggests washing out with weak boric acid and internal administration of cubebs, copaiba, sandal-wood oil, salol, benzoic acid, and so forth. Stone, and troublesome new growths, are to be removed by operation. When distress is extreme, Mackie and others have had good results from perineal cystotomy and drainage. Perineal fistula must be dealt with on ordinary surgical principles. Hyperplasia in the vagina and cervix is best treated by

Digitized by Google

scraping. Provided reinfection be avoided by the exercise of prudence in the matter of water, there is no necessity for sending the patient with this disease away from the country in which the parasite was acquired.

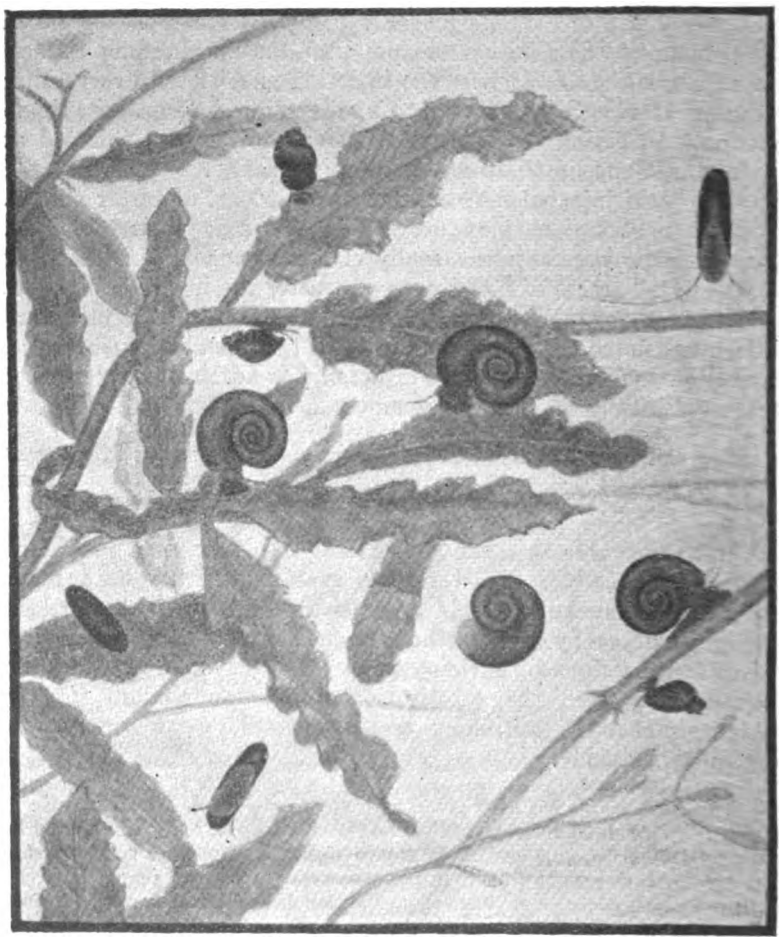


Fig. 128.—The intermediary hosts of S. hæmatobium and S. mansoni (Planorbis boissyi and Bullinus contortus) in their natural surroundings. Nat. size. (*J. K. Lund, del.*)

Prevention.—In the endemic districts, children, in particular, should be carefully and repeatedly warned against drinking or bathing in rivers, ponds, and canals. Sportsmen should be warned against wading, especially when engaged in shooting snipe, in

Digitized by Google

localities known to be infested; even fishing in fresh-water canals in countries like Egypt is not free from risk. Swamps, when slightly brackish, are safe. Seeing that the larva of schistosome, on obtaining access to fresh water, enters a fresh-water mollusc and, after undergoing developmental changes, obtains access to the human host, it is evident that if the larvæ be kept from getting into the water, or if drinking-water be boiled or filtered, the spread of the disease from man to man would be effectually prevented; therefore every care should be exercised to prevent the diffusion of the disease, by prohibiting the evacuation of excreta into, or near, water where the miracidia might find the opportunity of development and transmission. This prohibition should not be restricted to patients exhibiting definite symptoms of the disease, but extended to all, because, as special inquiries have shown, a large proportion of the infected do not suffer from any troublesome symptom and are often unaware of the infection. Leiper points out that much might be accomplished by attacking the mollusc intermediary and the free cercaria. As regards the former, he suggests periodic drying of irrigation canals and the use of chemical manures; and as regards the latter, the use of cercariacides such as sulphate-of-soda tablets for drinking-water, and boiling, and lysol, creolin, or cresol (1 : 10,000) for bathing-water. Chlorine in the strength (1 : 1,000,000) generally used in tropical countries to sterilize water appears to have no effect upon the living cercaria; the addition of larger quantities renders it unpotable. The free cercaria lives but a short time—at most forty-eight hours—in water, but a mollusc once infected continues to be so for months. The free cercariæ readily pass through the ordinary municipal filter-bed, for they can traverse 30 inches of fine sand in five hours; but they perish, as has been stated, if they do not get access to an appropriate host within forty-eight hours. These facts should be taken into account by the sanitarian.

II.—Intestinal Schistosomiasis

Schistosoma mansoni (Sambon), 1907

Definition.—A chronic endemic disease caused by *S. mansoni* (*Bilharzia mansoni*), giving rise to dysenteric and other symptoms referable to the intestinal canal, and characterized by the ova of the parasite in the fæces. In the early stages there may be general symptoms indicating absorption of the toxins of the adult parasites.

History and geographical distribution.—The occurrence

Digitized by Google

of a schistosome producing lateral-spined ova (Plate XXI., Fig. 2) was noticed by Bilharz in 1851, but he confounded it with *S. hæmatobium;* subsequently several observers encountered female worms with lateral-spined ova in utero, and the idea of a distinct species suggested itself to Sonsino and others, but this idea was at once discarded for other hypotheses. The lateral-spined ova being found only in the fæces of patients suffering from hæmaturia, the majority of physicians held that the peculiar position of the spine was due to distortion of the egg-shell in passing through the muscular coat of the rectum, forgetting that oviposition takes place in the submucous layer, and that lateral-spined ova are found in the uterus of the parent worm. Sonsino suggested that the two kinds of eggs might represent respectively male and female embryos, and Looss that they were the product of unfertilized females.

In 1903, in examining a patient who had long resided in Antigua and other West India Islands and who had never visited Africa, Manson found in his fæces numerous ova all bearing a lateral spine. Repeated examination of the urine proved negative, and the patient stated that he had never at any time suffered from hæmaturia. This case, together with the absence of endemic hæmaturia in the West Indies, led him to think that probably the lateral-spined ova indicated a distinct species of schistosome. Since then this conjecture has proved to be correct. A new species of schistosome (*S. japonicum*), with what are practically spineless ova, and affecting the intestine principally, had been discovered in Japan, and careful examinations for helminths in the Congo Free State and in Porto Rico showed the absence of urinary schistosoma disease and the frequency in these regions of a rectal schistosoma infection in which the ova of the parasite invariably bore a lateral spine. Finally, in 1907, Sambon, having had the opportunity of comparing specimens of the type characterized by lateral-spined ova with *S. hæmatobium* and other Schistosomatidæ, and taking into consideration its peculiar geographical distribution and distinct pathogeny, proposed that it should be ranked as a distinct species and named it *S. mansoni.* Since that time many cases of lateral-spined intestinal schistosomiasis have been reported from South America by Flu.

Holcomb and da Silva first described the anatomical distinctions between the adult *S. mansoni* and *S. hæmatobium.* It may be said, however, that the duality of the species remained undecided until 1916, when Leiper proved beyond doubt that the miracidia hatching from lateral-spined eggs developed only in the planorbis

Digitized by Google

snail and gave rise to cercariæ which developed into adults with constant morphological distinction. Since that time this work has been confirmed by Fairley and the Editor in Egypt and by Lutz in Brazil. It is surmised that this schistosome is a West African species, and was originally imported into the western hemisphere by African negroes. The geographical distribution of this species, as far as is known at the present day, extends from the Nile Valley, throughout Central and West Africa, the West Indies, and South America; most probably its range of distribution is limited by that of an appropriate intermediary host of the genus *Planorbis*. (Fig. 129.)

Etiology.—The anatomical characteristics of *S. mansoni* have already been referred to (p. 560); it only remains to be stated that the males are generally of smaller size than those of *S. hæmatobium*, and more grossly tuberculated. The female deposits but one or two ova at a time; this fact is explained by the

Fig. 129.—Planorbis boissyi. Nat. size. (*After Leiper.*)

anatomical structure of the uterus. The *ova* are somewhat spindle-shaped and are provided with a lateral spine. (Plate XXI., Fig. 2.) They are generally slightly shorter than those of *S. hæmatobium*, 0·15 mm. in length by 0·056 mm. in diameter. These ova are passed out in the fæces, though rarely in the urine, and hatch out a ciliated miracidium. According to Cort, the cephalic glands of the miracidium are somewhat larger, in proportion to the length of the body, than in the case of the embryos of the other two species of human schistosomes.

The *cercariæ* differ in a few minor respects from those of *S. hæmatobium*; they are slightly shorter and the ventral sucker is not so prominent. (Fig. 124, 1.)

Symptoms.—*S. mansoni* inhabits chiefly the branches of the portal vein in the liver, and the mesenteric veins. Its ova, deposited within the submucous layer of the rectum, give rise to dysenteric-like symptoms, mucus with blood being passed from time to time, and the ova-laden stools becoming frequent and their passage perhaps being attended with tenesmus. In certain well-

Digitized by Google

established cases small (sometimes large), branching, soft growths are to be felt inside the sphincter ani. They resemble polypoid growths and are apt to be mistaken for piles. They may extend as high up the bowel as the sigmoid flexure. On tearing up one of these growths one can see the ova in the débris. (Fig. 130.)

In mass infestations, in early cases, toxic symptoms resembling those of Katayama disease (p. 579) were noted in 1916 in Australian and Imperial troops stationed in Egypt. The general symptoms consisted of a remittent pyrexia, with urticaria, marked abdominal pain, anorexia, rigors, and pulmonary symptoms. A pronounced

Fig. 130.—Rectal schistosomiasis: adenomata prolapsed through anus. (*After Madden.*)

leucocytosis with a high eosinophilia (up to 76 per cent.) was noted. (Chart 27.)

Later, localized symptoms with passage of dysenteric motions supervened. These cases were at first mistaken for enteric or for hepatic abscess.

In the terminal stages of the disease large abdominal tumours may form, easily palpable, and actual intestinal stasis or distension may take place. Infiltration of the buttocks with ova, leading to induration and fistulæ, is not uncommon. When the liver has become markedly cirrhotic, ascites may be present. Pneumonia from ova-deposition in the lungs is an occasional complication. Sometimes the dysenteric attacks may develop into acute diarrhœa of a choleraic type, which may prove fatal.

Pathological anatomy.—The eggs of *S. mansoni* may be

Digitized by Google

found in great numbers in the liver, where they give rise to a peculiar form of "pipe-stem" cirrhosis. It is possible that further investigation may prove that a finer grade of fibrosis, due to the absorption of the schistosoma toxins and the irritation produced by the ova, exists in a considerable proportion of infestations, and may in fact be responsible for the frequency of cirrhosis of the liver in Egypt. Sandy patches, due to the deposition of calcified ova, cover large areas of the intestinal surface, and may give rise to acute choleraic diarrhœa during life. Deposits of black pigment granules take place in the interstitial and secreting cells of the liver, and have been shown by Fairley to take place in both *S. mansoni* and *S. hæmatobium* infestations, but to be commoner and more abundant in the former. This pigment he believes to be hæmatoidin, since it gives the typical reactions. The coats of the large intestine are, as a rule, hypertrophied and the mucosa the seat of dark-red or brown massive polypoid pseudo-adenomata, which bleed easily. These growths are apt to ulcerate and involve considerable areas of the mucous surface. Cell accumulations or pericolonic nodules occur on the peritoneal surface, as well as in the mesentery. The lymph-glands in the latter situation and in the retroperitoneal tissue are enlarged, and there is generally an appreciable hypertrophy of the spleen, which, seeing that ova are not generally found in this situation, is attributable to toxic absorption.

Diagnosis.—The characteristic ova are easily found in the fæces under a low power of the microscope; they may be very scanty, and it is necessary to examine three or more specimens before arriving at a negative diagnosis. (Fig. 131.) They are more easily found in solid than in fluid motions, especially in the outer portions of a scybalus. It must be remembered that quite a high proportion of cases are latent ones—that is to say, they do not present any of the more urgent symptoms. In about 50 per cent. of cases Bandi and Fairley have shown that the characteristic ova may be found in the urine as well as in the fæces.

The complement-deviation reaction is the same as in *S. hæmatobium* infestations.

In rectal disease, should *S. mansoni* be suspected, one of the adenomatous growths may be removed by means of a forceps and examined for ova.

Sigmoidoscopic examination may reveal the pedunculated adeno-papillomata situated in the upper portion of the rectum, but usually this is unnecessary, as they can be felt by digital examination alone and may be seen protruding in polypoid masses from the anus. The localized thickening of the large intestine,

Digitized by Google

due to polypi and pericolonic growths, can be palpated in heavily infested subjects through the abdominal wall. They are more generally situated in the transverse and pelvic colon than elsewhere.

Treatment.—Gross changes in the organs are more extensive than in *S. hæmatobium* infestations, due partly to toxic absorption and partly to deposition of ova. Madden and Day have recently reported from Egypt that it is possible, as in the former case, for the adult worms to be killed by *tartar emetic* treatment, but the

Fig. 131.—Microphotograph of miracidium of Schistosoma mansoni escaping from ovum. × 1,500. (*By permission of Dr. A. J. Chalmers.*)

effects of their presence remain. Hence it may prove necessary to operate upon polypoid or adenomatous growths obstructing the intestinal lumen. In early cases antimony is as successful as it is against *S. hæmatobium*.

Prognosis.—This is probably the same as for *S. hæmatobium*, but it must be remembered that the disease generally assumes a latent form, and that even large intestinal polypi may give rise to little or no inconvenience. Those cases with actual obstruction of the intestinal canal and cirrhotic changes in the liver must be regarded as serious.

Digitized by Google

Prevention.—This is the same as in the case of the urinary form. There appears to be a greater probability of contracting the disease in the neighbourhood of muddy canals which are the favourite haunt of planorbis, of which a high proportion (50 per cent. or more in some cases) are found to be infested with cercariæ of this trematode in Egypt.

III.—Schistosomiasis of the Far East

Schistosoma japonicum (Katsurada, 1904)

Synonyms.—*S. cattoi;* Katayama Disease.

Definition.—A chronic endemic disease of Eastern countries, caused by *S. japonicum*, characterized by great enlargement of the liver and spleen and development of ascites. The ova of the parasite are discharged in the fæces. Initial toxic symptoms with urticaria and pyrexia are commonly observed.

History and geographical distribution.—For some years Japanese physicians had observed in the provinces of Yamanashi and Hiroshima in Central Japan, and at Saga in the North Island, an endemic disease characterized by enlargement of the liver and spleen, cachexia, and ascites. The patients suffered from diarrhœa, their motions containing mucus tinged with blood. Occasionally they had fever. They became anæmic, and many of them died from exhaustion. At the autopsy the liver and other organs were found to contain the ova of some unknown helminth. As far back as 1888 Majima, in Tokio, found peculiar ova of an unknown parasite in the liver of a case of cirrhosis; an observation confirmed by Yamagiwa in 1890. In 1904 Katsurada discovered that the eggs in the stools of these patients contained a ciliated embryo not unlike the miracidium of *S. hæmatobium*, and further he found adult trematodes (*S. japonicum*) in the portal veins of the cat; later in that year Catto noted similar parasites at a human autopsy. Examining dogs and cats in the endemic area, Katsurada had the good fortune to find in the portal system of two cats from the province of Yamanashi numerous schistosomes containing eggs exactly similar to those previously found in man. He published this information on August 13th, 1904, and named the new trematode *S. japonicum*. Almost simultaneously, and independently, Fujinami observed cases of the disease in the village of Katayama, in the province of Bingo, and found in his first fatal case the characteristic ova in various organs. Then Katsurada succeeded in communicating the parasite to cats by immersing their legs in the water of certain ponds and streams reputed to convey the disease; and finally, in 1913, Miyairi and Suzuki traced the

Digitized by Google

parasite, through a snail common in the infected districts, back to the vertebrate host.

The geographical distribution of *S. japonicum* is probably a fairly wide one and coincides with that of its intermediary host. So far, the parasite has been found principally in Chinese and Japanese, though a few Europeans, mostly naval officers and sportsmen addicted to snipe-shooting in the rice-fields, have acquired the disease. Its present range may be stated as follows: In China it occurs in endemic foci in the Yangtse basin, in the provinces of Hunan, Honan, Hupeh, Anhui, and Kiangsi. In Japan it is especially prevalent in the province of Hiroshima and in the village of Katayama, whence the disease originally received its name. Endemic foci also exist in the Philippine Islands, for the most part in those of the southern group, Samar, Leyte, and Mindanao. In the countries where it exists, domestic animals, dogs, cats, and cattle, are found naturally infected.

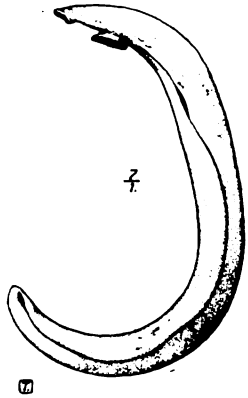


Fig. 132.—Schistosoma japonicum (male).

The parasite (Fig. 132).—*S. japonicum* closely resembles in general structure *S. hæmatobium*. As in the latter, the suckers are placed close together at the anterior extremity of the body, the acetabulum or posterior sucker being distinctly pedunculated and funnel-shaped. The suckers in both sexes and the ventral surface of the body in the male are provided with minute spines. The distinctive characters are its smaller dimensions (male, 9 to 12 mm. in length by 0·5 mm. in breadth; female, 12 mm. in length by 0·4 mm. in breadth),* and the larger size of the acetabulum as compared with the oral sucker; both are relatively larger than those of *S. hæmatobium*. In the male the integument is smooth and non-tuberculated, and the posterior part of the body in the male is relatively wider, the sides overlapping one another far more extensively than in *S. hæmatobium*. The œsophagus is provided with two bulbs; the bifurcation of the alimentary canal takes place, as in *S. mansoni*, at the level of the ventral sucker, but the union of the intestinal cæca is effected more posteriorly; the united gut occupying a quarter to one-fifth of the total body length. The excretory system consists of two longitudinal canals opening posteriorly and dorsally by the excretory pore.

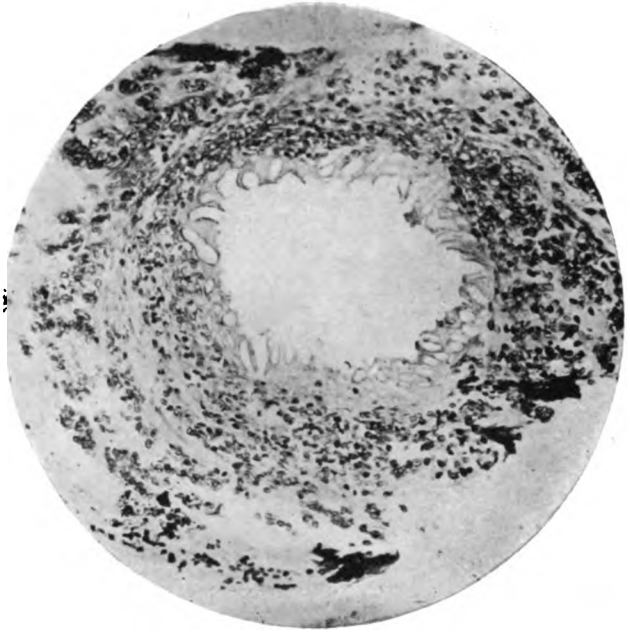
The *male* has six to eight elliptically shaped testes situated dorsally to the acetabulum. The vasa efferentia join to form a common duct opening directly posterior to it; there is also a large seminal vesicle.

The *female* is considerably thinner than the male; the ovary is situated

* A great variation in length is noticeable in figures given by various authors for the worm. Katsurada has reported both males and females up to 20 mm. in length.

Digitized by Google

Schistosoma japonicum in vessels of mesentery.
(*Microphoto: Dr. Henderson.*)



Eggs of Schistosoma japonicum embedded in walls of appendix vermiformis. (*Microphoto: Dr. Kerr.*)

SCHISTOSOMIASIS OF THE FAR EAST.

PLATE XXII.

Digitized by Google

Digitized by Google

in the middle of the body. The gut branches unite immediately behind it. The yolk-glands, well developed, extend almost to the posterior extremity. The uterus also is well developed, and occupies the anterior portion of the body; it may contain 50 to 300 ripe ova.

The habitat of the worms is the smaller mesenteric blood-vessels (Plate XXII., Fig. 1), especially those draining the large intestine. Immature examples may be present in the portal and splenic veins, also in the gastric veins and in the coats of the small intestine, and even in the coronary veins of the heart; in cattle, but not in man, they have been found occupying the pulmonary artery. The life-span of the adult worm is probably as long as that of *S. hæmatobium*.

Fig. 133.—Egg of Schistosoma japonicum, showing characteristic lateral knob. (*After Leiper.*)

Probably the *ova* are extruded from the blood-vessels in the same manner as has been described for *S. hæmatobium* and *S. mansoni*; they are found chiefly in the walls of the intestine, the liver, pancreas, and mesenteric glands. They are 40 to 60 μ in length and 38 to 40 μ in breadth, are smooth and possess no spine; but they possess, as Leiper has pointed out, what may pass for a rudimentary lateral spine in the form of a very minute and easily overlooked papilla—like an excrescence, in a cup-like depression in the shell. The ova are said to enlarge during their passage through the tissues, and may eventually reach a length of 90 μ. (Fig. 133, and Plate XXII., Fig. 2.)

The ova are discharged in the fæces of the vertebrate host. In this way they get carried to water, where the ciliated miracidium escapes; in it the

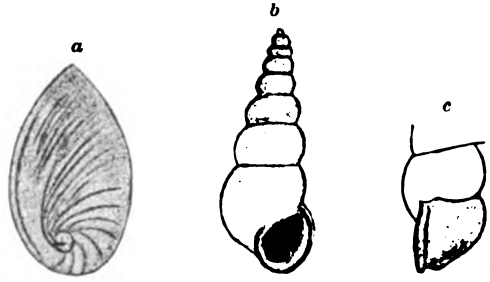


Fig. 134.—Operculum and shell of Hypsobia (Blanfordia) nosophora. (*After Robson.*)

a, Operculum, × 12, diagrammatic to show scheme of coiling; *b*, oral aspect of shell, × 4; *c*, lateral aspect of shell, showing labial swelling, × 4.

cephalic glands are, according to Cort, perceptibly smaller than in the *S. mansoni* or in *S. hæmatobium* miracidium. In 1913 Miyairi and Suzuki traced the development of the ciliated miracidium in a fresh-water mollusc, *Hypsobia* (*Blanfordia*) *nosophora* (Fig. 134), wherein, after shedding its cilia, it becomes a sporocyst (Fig. 135, *a*). In the liver and hermaphrodite gland numbers of fork-tailed cercariæ are ultimately developed (Fig. 135, *b*). The *cercariæ* are smaller than those of *S. hæmatobium* or *S. mansoni*, and are 0·25 mm. in length and 0·04 mm. in breadth. The body is covered with minute spines.

Digitized by Google

The oral sucker is greatly developed, occupying the anterior third of the body, and, as in the other schistosome cercariæ, is provided at its free edge with a number of minute papillæ. There are five pairs of cephalic, or salivary, mucin glands. (Fig. 124, 3.) On maturity the cercariæ escape into the water and, opportunity presenting, penetrate the skin of some appropriate vertebrate (man, cat, dog, mouse, etc.), in which they attain sexual maturity. The sporocysts of *S. japonicum* are said to be more delicate and elongated than are those of the other two species. These observations have been confirmed by Leiper.

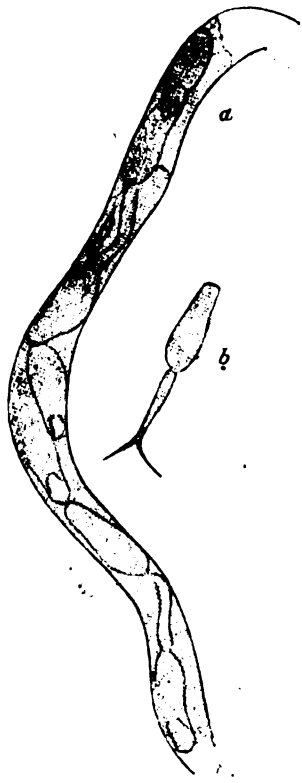


Fig. 135.—*a*, Sporocyst of S. japonicum, from Hypsobia nosophora, × 100; *b*, cercaria from the sporocyst, × 100. (*After Leiper.*)

Hypsobia nosophora, belonging to the Hydrobiidæ and of the Pectinibranchiate order, is a dark-grey snail, sharply conical, with a dextral opening, and is peculiar to the Yangtse valley and Japan. It is 6·7–9 mm. long by 2·4–3·4 mm. broad. The coils number 8–8½.

Morbid anatomy.—The outstanding feature is the great enlargement of the liver and spleen; the former is hypertrophied and nodular from the formation of and contraction by fibrous tissue, and on digesting with 3-per-cent. potash solution is found to contain many ova. The great enlargement of the spleen, on the other hand, is probably due to absorption of toxins, or is possibly the result of back pressure, as ova are seldom found in this organ, but granules of black pigment are found in both viscera. Possibly, as in *S. mansoni*, many of the widespread changes are the result of toxæmia. The ascites is probably due to portal stasis. The appendices epiploicæ are greatly thickened and may be matted together; the mesenteric and retroperitoneal lymph-glands are enlarged; hypertrophy and thickening of the lower parts of the intestinal tract with formation of ulcers and polypoid growths in the lumen are generally noted. The bladder is unaffected.

Occasionally, indurations of the pia mater and lesions of the cortex of the brain have been found.

Symptoms.—The disease produced by *S. japonicum*, some-

Digitized by Google

times called "Katayama disease," is a serious one and, when pronounced, proves fatal sooner or later. The gravity of any given case will depend, amongst other things, on the degree of infection and the circumstances of the patient. Of 1,077 persons near Shushima, Japan, examined by Koiki, 42 were found infected. Of these 42, only 22 were not in good health.

The course of the disease can be divided into three stages. The *first* occurs within a short period of infestation and lasts about a month. It is associated with toxic symptoms, such as pyrexia, urticaria, abdominal pain, paroxysmal cough, and a high eosinophilia (60 per cent. or more). The *second* stage is characterized by great emaciation and is accompanied by dysenteric symptoms and enlargement of the liver and spleen. The *third* or final stage, when it does supervene, occurs from three to five years after infestation. In this the liver is cirrhotic and enlarged. Ascites and œdema of the extremities appear, with anæmia and exacerbations of the dysenteric symptoms. (Fig. 136.) The patient may die of exhaustion or of some terminal infection. Jacksonian fits, due to deposition of ova in the brain cortex, and hemiplegia have been described.

Fig. 136. — Asiatic schistosomiasis. (*Photo: Dr. J. A. Thomson; courtesy of Wellcome Bur. Sci. Res.*)

Penetration of the skin by the cercariæ causes an intense pruritus, partly mechanical, and partly due to an irritating substance secreted by the larvæ. The erythema thus produced was regarded by the Japanese as a skin disease, "kabure." The same thing happens after infestation with the cercariæ of the other two human schistosomes—*S. mansoni* and *S. hæmatobium*.

Diagnosis.—All cases of urticarial fever from the endemic districts should be watched for many months, especially if eosinophilia persists after the subsidence of the primary attack, and the stools examined for ova of *S. japonicum*. All cases of chronic intestinal disturbance, especially if associated with enlargement of

Digitized by Google

liver and spleen, from the districts mentioned should be regarded as, possibly, cases of schistosomiasis, and the blood and stools should be examined. If the ova (Fig. 137) are discovered the diagnosis is established.

A complement-deviation reaction, as in *S. hæmatobium*, with antigen made from cercariæ, may be employed. Suezasu in 1917 produced an antigen from the bodies of the adults and obtained a positive complement deviation with the serum of an artificially infested horse.

Treatment.—It is more than probable that antimony will

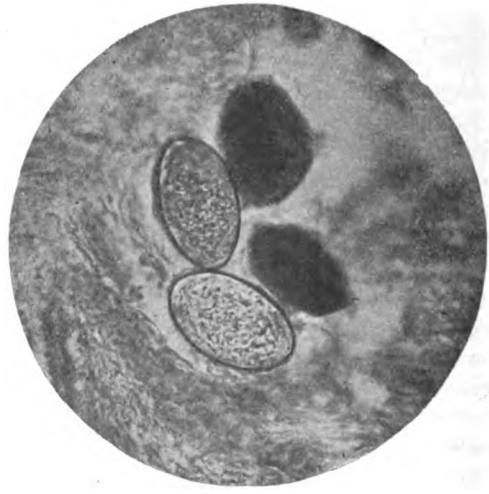


Fig. 137.—Eggs of S. japonicum in fæces. × 250. (*Photo: Dr. J. Bell.*)

prove to be as efficacious in this helminthiasis as it is known to be in *S. hæmatobium*.

Prevention.—Water reported to cause the disease should be boiled, or avoided, for drinking or bathing purposes. Sportsmen, if they must wade in such waters, should wear long boots or waterproof waders. According to Narabayashi, lime is the most economical reagent available for the extermination of the intermediary host. The cercariæ are photophobic, and are easily killed by temperatures higher than 50° C., as well as by 10-per-cent. salt solution and by artificial gastric juice. Lime solution, 1 : 1,000, kills the cercariæ in thirty minutes, and because of its value as a fertilizer its use is recommended as a practical measure.

Digitized by Google

CHAPTER XLI

PARASITES OF THE LYMPHATIC SYSTEM AND CONNECTIVE TISSUES

FILARIASIS

History.—Our knowledge of this subject dates from the discovery by Demarquay, in 1863, of a larval nematode—*microfilaria bancrofti* (Plate XXIII.)—in the milky fluid from a case of chylous dropsy of the tunica vaginalis. Later, in 1866, Wücherer found the same organism in the urine of a number of cases of chyluria. In 1870 Lewis made a similar observation in India, and in 1872 discovered that the blood of man is the normal habitat of this larval parasite, which he named, accordingly, *Filaria sanguinis hominis*. Four years later, Bancroft in Brisbane (Queensland) discovered the adult form, and Cobbold named it *Filaria bancrofti*. In 1878 Manson discovered that the mosquito subserved the filaria as intermediary host, and in 1880 he described the phenomenon of filarial periodicity. Since that time the subject has rapidly expanded, and the great practical importance of the filaria in tropical pathology is now recognized.

Nomenclature of the parasites.—Manson originally pointed out that Lewis's microfilaria (a term suggested by Le Dantec to designate the larval forms of the various nematodes whose young circulate in the blood, and adopted in this manual) is not the only blood-worm in man, and that the human circulation is the habitat of the larvæ of no fewer than five, possibly of six or even more, distinct species of filariæ. In consequence of this discovery it was deemed advisable to modify the original name of Lewis's microfilaria. This Manson proposed to call *Filaria nocturna ;* but as, in accordance with the rules of zoological nomenclature, precedence must be given to the name previously suggested by Cobbold for the adult form, the embryonic form is now known as *microfilaria bancrofti* (Plate XXIII., Fig. 1). The other filariæ of the blood are named *microfilaria diurna* (or *mf. loa*) (Plate XXIII., Fig. 3), *microfilaria ozzardi* (*mf. demarquayi*) (Plate XXIII., Fig. 4), *microfilaria perstans* (Plate XXIII., Fig. 2).

Their pathological importance.—Only one of these parasites, so far as we know at present, appears to have important pathological

Digitized by Google

bearings—*Filaria bancrofti*, which, in its adult stage, inhabits the lymphatics of man. As regards the others, with the exception of *Loa loa*, *Onchocerca volvulus*, and *Dracunculus medinensis*, we have no knowledge of any serious pathological significance they may possess. There can be no question of the importance in tropical pathology of *F. bancrofti*; there is abundant reason to believe that it is the cause of endemic chyluria, of various forms of lymphatic varix, and of other obscure tropical diseases, including tropical elephantiasis.

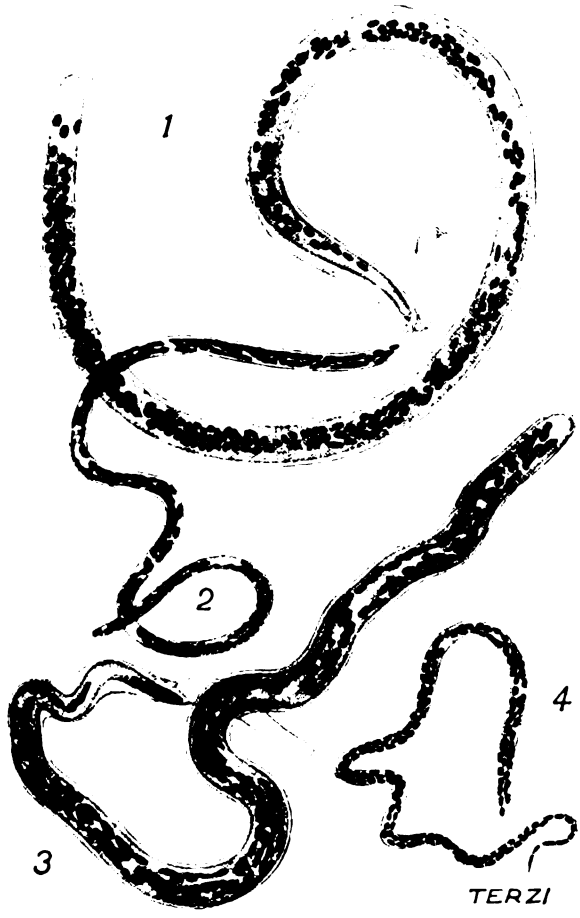
The filariæ less important from a pathological standpoint are dealt with in the Appendix (pp. 838–44).

1. Filaria bancrofti (Cobbold, 1877)

Geographical distribution and prevalence.—The geographical distribution of *F. bancrofti* is very extensive. It has been found as an indigenous parasite in almost every country throughout the tropical and subtropical world, as far north as Spain in Europe and Charleston in the United States of America, and as far south as Brisbane in Australia. In many places—South China, for example—quite 10 per cent., and in other places half of the population harbour it. Manson has ascertained that it is probable that one-third of the inhabitants of at least one district in India—Cochin—carry blood microfilariæ; similarly in some of the South Sea Islands—Samoa, for example—fully one-half of the people are affected in this way. Thorpe has shown that in the Friendly Islands 32 per cent., and the Editor has found that in the Fiji group 27·1 per cent. of the inhabitants harbour this microfilaria in the bloodstream, while another 25·4 per cent. show abundant evidence of filarial disease—that is to say, 52·5 per cent. of the inhabitants are probably infested with the parasite. In one particular island of this group no less than 75 per cent. of the natives are affected. We have similar testimony as to the great frequency of the parasite in Madras from Maitland and others, in Demerara from Daniels, in several of the West India Islands from Low, in West Africa from Annett, Dutton, and Prout. Doubtless, if diligently and systematically sought for, it could be found in most tropical countries.

Demonstration of blood microfilariæ.—Whoever would investigate the subject of filariasis will find that, in order practically to comprehend the subject and to provide himself with abundant material for observation, it is advisable to make systematic examination of the blood of the inhabitants of some district in which filariasis is endemic. If this be done, the observer is sure, sooner

Digitized by Google



1, Mf. bancrofti; 2, mf. perstans; 3, mf. loa; 4, mf. ozzardi.

MICROFILARIÆ OF THE BLOOD.

PLATE XXIII.

Digitized by Google

Digitized by Google

or later, to come across cases in which *microfilaria bancrofti* abounds, and also of the diseases to which the parental form gives rise.

Technique of blood examination for microfilariæ.—Microfilariæ, when present in large numbers in the bloodstream, may easily be recognized in a wet film preparation under the microscope. For dried preparations it is desirable to take quite a considerable quantity of blood. (For details regarding the preparation of the film and methods of staining, *see* Appendix III., p. 880.)

Description of embryonic form.—Examined in fresh blood, *microfilaria bancrofti* (Fig. 138) is seen to be a minute, transparent, colourless, snake-like

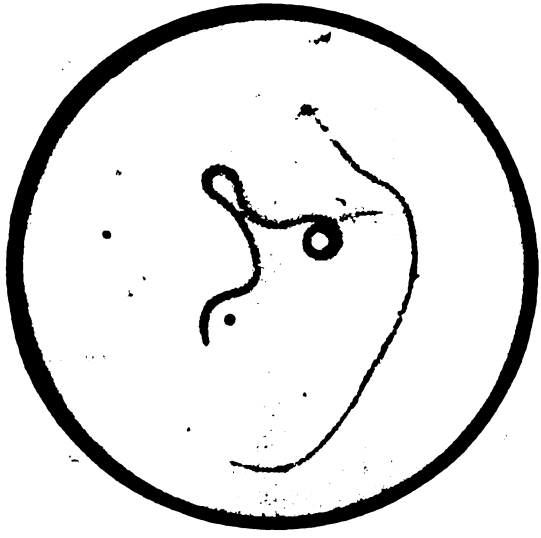


Fig. 138.—Mf. bancrofti in hydrocele fluid. The embryo on the right has escaped from its sheath. (*Orig.*)

organism, which, without materially changing its position on the slide, wriggles about in a state of great activity, constantly agitating and displacing the corpuscles in its neighbourhood. At first the movements are so active that the anatomical features of the microfilaria cannot be made out. In the course of a few hours the movement slows down, and then one can see that the little worm is shaped like a snake or an eel; that is to say, that it is a long, slender, cylindrical organism, having one extremity abruptly rounded off, and the other for about one-fifth of the entire length gradually tapered to a fine point. On measurement, it is found to be a little under 0·3 mm. in length by 0·006–0·008 mm. in diameter—about the diameter of a red blood-corpuscle.

When examined with a low power, it appears to be structureless; with a high power a certain amount of structure can, on close scrutiny, be made

Digitized by Google

out. In the first place, it can be seen that the entire animal is enclosed in an exceedingly delicate, limp, structureless sack, in which it moves backwards and forwards. This sack, or "sheath," as it is generally called, although closely applied to the body, is considerably longer than the worm it encloses; so that that part of the sack which for the time being is not occupied is collapsed and trails after the head, or tail, or both, as the case may be. It can be seen also that, about the posterior part of the middle third of the parasite, there is what appears to be an irregular aggregation of granular material which, by suitable staining, can be shown to be a viscus of some sort. This organ runs for some distance along the axis of the worm. Further, if a high power be used, a closely set, very delicate transverse striation can be detected in the musculo-cutaneous layer throughout the entire length of

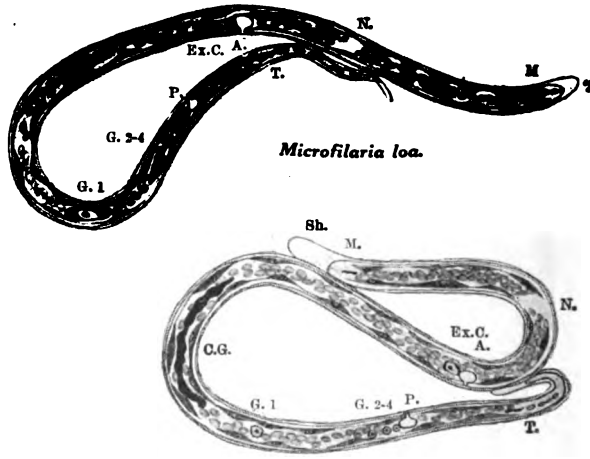


Fig. 139.—Minute anatomy of a microfilaria, and differential points of structure between mf. loa and mf. bancrofti. (*After Fülleborn.*)

N., Nerve ring (ant. break in cell column); A., ant. V-spot (exc. pore); EX.C., excretory cell; C.G., granular mass (or Innenkörper); G. 1–4, genital cells; P., posterior or tail spot; M., granules in mouth cavity; T., granules in tail; SH., sheath.

the animal. Besides this, if carefully looked for at a point about one-fifth of the entire length of the organism backwards from the head end, a shining, triangular V-shaped patch is always visible. What may be this V spot is brought out by very light staining with dilute logwood. The dye brings out yet another spot similar to the preceding, though very much smaller; this second spot is situated a short distance from the end of the tail. The former has been designated the "V spot," the latter the "tail spot." These spots are probably connected with development, the V spot being the rudiment of the future water-vascular system, the tail spot that of the anus or cloaca and terminal part of the alimentary canal. The spots are not stained by strong logwood nor by the aniline dyes. Staining with logwood also shows that the body of the little animal is principally composed of a column of closely packed, exceedingly minute cells enclosed in a transversely striated

Digitized by Google

musculo-cutaneous cylinder; at all events, many nuclei are thereby rendered visible. Low has pointed out that the break seen in all stained specimens in the central column of nuclei occurs at a point slightly anterior to the V spot. This break can only be recognized in stained preparations.

Rodenwaldt and Fülleborn, by careful study of specially stained specimens, have further elucidated the histology of the microfilaria, which is fully illustrated in Fig. 139 (borrowed from Fülleborn), special attention being directed to the excretory and genital cells and substances in the rudimentary intestinal canal. (*See also* Plate XXIII.)

When the movements of the living microfilariæ have almost ceased, by careful focusing it can be seen that the head end is constantly being covered and uncovered by a six-lipped—or hooked—and very delicate prepuce; and, moreover, one can sometimes see a short fang of extreme tenuity, based apparently on a highly retractile granule, suddenly shot out from the uncovered extreme cephalic end, and as suddenly retracted (Fig. 140), and in a

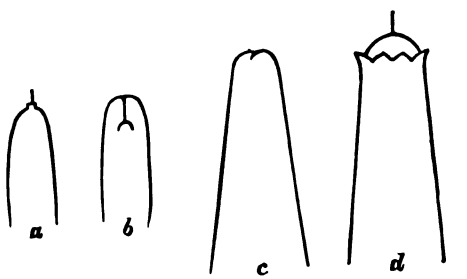


Fig. 140.—Structure of head end of mf. perstans (*a*, *b*) and of mf. bancrofti (*c*, *d*).

fresh blood preparation it can be seen disturbing the red cells at some distance away. This delicate organ is difficult to stain, but that it can be done by appropriate technique is shown by the microphotograph reproduced in Fig. 141, which was obtained by staining with Leishman's stain in the first instance, and subsequently with hæmatoxylin.

Filarial periodicity.—A singular feature in the life of the microfilaria is what is known as "filarial periodicity."

If under normal conditions of health and habit the blood be examined during the day, the parasite is rarely seen, or, if it be seen, only one or two specimens at most are encountered in a slide. It will be found, however, that as evening approaches, commencing about five or six o'clock, the microfilariæ begin to enter the peripheral circulation in gradually increasing numbers. The swarm goes on increasing until about midnight, at which time it is no unusual thing to find as many as three hundred, or even six hundred, in every drop of blood; so that, assuming that the parasites are evenly distributed throughout the circulation, it may be inferred

Digitized by Google

that as many as forty or fifty millions are simultaneously circulating in the blood-vessels. After midnight the numbers begin gradually to decrease; by eight or nine o'clock in the morning the microfilariæ have disappeared from the peripheral blood for the day. This nocturnal periodicity, under normal conditions, is maintained with the utmost regularity for years. Should, however, as Mackenzie has shown, a filarial subject be made to sleep during the day and remain awake at night, the periodicity is reversed; that is to say, the parasites come into the blood during the day

Fig. 141.—Microfilaria bancrofti, showing spicule. × 1,000. (*Original preparation.*) (*Microphoto: Dr. A. Norman.*)

and disappear from it during the night. It cannot be the sleeping state, as some have conjectured, that brings about this periodicity; for the ingress of the microfilariæ into the peripheral blood commences three or four hours before the usual time for sleep, and the egress several hours before sleep is concluded, and this egress is not complete until several hours after the usual time of waking. This night swarming of the embryos of *F. bancrofti* in the peripheral circulation is an adaptation correlated to the life-habits of its liberating agent, the mosquito *Culex fatigans*, its usual intermediary host. (Chart 30.)

Digitized by Google

Thirty years ago Manson had an opportunity of ascertaining that during their diurnal temporary absence from the peripheral circulation the microfilariæ retire principally to the larger arteries and to the lungs, where, during the day, they may be found in enormous numbers.

The patient on whom this observation was made was the subject of lymph scrotum and varicose groin glands. His blood contained large numbers of embryo filariæ which exhibited the anatomical features and periodicity characteristic of *microfilaria bancrofti*. One morning he committed suicide by swallowing a large quantity of dilute hydrocyanic acid. Death was almost instantaneous. At the post-mortem examination, made six hours later, a huge lymphatic varix was found occupying the pelvis and back part

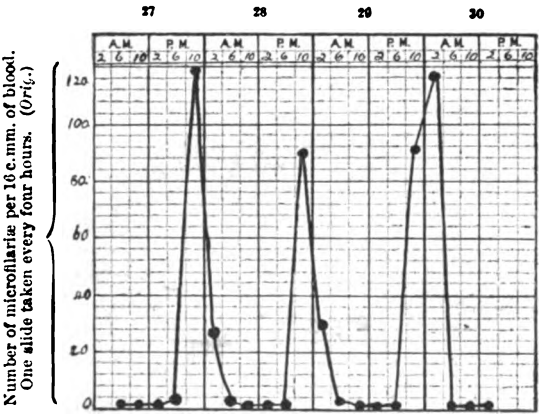


Chart 30.—Filariasis (F. bancrofti, microfilaria nocturna), showing nocturnal periodicity.

of the abdominal cavity. In the dilated lymphatic vessels many adult filariæ—*F. bancrofti*—were found. The distribution of the microfilariæ was studied by counting them in drops of blood expressed from the various organs, and also in sections. The result is summarized in the following tables :—

ENUMERATION OF MICROFILARIÆ IN A DROP OF BLOOD EXPRESSED FROM THE FOLLOWING ORGANS

Organ	No. of slides	Aggregate No. of microfilariæ	Average per slide
Liver	3	2	1
Spleen	3	3	1
Brachial venæ comites ...	4	111	28
Bone-marrow	1	0	0
Muscle of heart	3	365	122
Carotid artery	1	612	612
Lung	10	6,751	675

Digitized by Google

ENUMERATION OF MICROFILARIÆ IN SECTIONS OF THE FOLLOWING ORGANS

Organ	No. of sections	Aggregate No. of microfilariæ	Average per section
Liver	10	3	0·3
Spleen	4	0	0·0
Kidney	8	13	1·6
Brain	4	4	1·0
Muscle (voluntary)	3	2	0·33
Heart muscle	4	68	17·0
Lung	6	301	50·16
Lobe of ear	4	1	0·25
Scrotum	4	0	0·0

In the lung sections (Fig. 142) the microfilariæ lay outstretched or variously coiled in the vessels, large and small. In the heart muscle they lay along the capillaries between the fibres; in the kidneys they seemed specially to affect the Malpighian tufts; a very few were found in the capillaries of the brain; vast numbers were found in smears from the inner surface of the

Fig. 142.—Section of lung showing microfilariæ in the blood-vessels. (*Microphoto: Dr. Spitta.*)

carotid arteries. The preparations afforded no explanation as to how the microfilariæ contrive to maintain their position in the blood current, or as to the forces determining their peculiar distribution.

Subsequent observations by the Editor in Fiji have shown that the microfilariæ can be demonstrated in the capillaries of the liver and spleen in small numbers. The capillaries of the lung appear to be the favourite habitat of other microfilariæ. *Microfilaria immitis*, *mf. perstans*, and the non-periodic Fijian microfilariæ have been found in greatest abundance in this situation.

Digitized by Google

Various theories have been advanced by Fülleborn and others to account for this singular phenomenon, though none are entirely satisfactory. Yorke and Blacklock think that obstruction to the passage of microfilariæ through the cutaneous vessels is at a minimum at the end of the period of bodily activity, and that the periodicity is primarily dependent upon the variations in the actual supply of microfilariæ to the cutaneous vessels. But how account for the diurnal periodicity of *microfilaria loa* under circumstances exactly the reverse of this, or for the non-periodic form of *F. bancrofti*?

Non-periodic microfilaria bancrofti. — Until recently it was believed that, in normal conditions of health and habit on the part of the human host, nocturnal periodicity was uniformly observed by the microfilaria of *Filaria bancrofti* at all times and in every country. Many years ago Thorpe remarked that in Tonga and Fiji the filaria could be found often in great abundance in the blood during the daytime; and in 1906 Ashburn and Craig found a microfilaria in the Philippines, morphologically identical with *microfilaria bancrofti*, which showed no periodicity, and which these authors, relying on this feature, considered a distinct species and named *F. philippinensis*. Wilson, in 1909, after a systematic study of the point in a considerable number of cases in Fiji, also considered that the local filaria was non-periodic—an observation amply confirmed by the Editor in 1910. Similarly, Fülleborn found that the microfilaria of Samoa showed no periodicity. Strange to say, the filaria of neighbouring islands in the Pacific—namely, the Solomons, New Guinea, and the Bismarck Archipelago—are strictly periodic in their blood appearances.

The Editor has shown that the filariæ of Indian immigrants who have acquired their filarial infections in India retain their periodic habits during at least three years of residence in Fiji, and that if an Indian or a Solomon Islander acquires the infection in Fiji the microfilariæ are non-periodic in habit. Connal and Thiroux, in a proportion of instances of filarial infection in West Africa, have found the microfilariæ to be non-periodic, whilst in other instances they exhibit the nocturnal habit just as those of India, China, and America are known to do. In natives of Northern Nigeria the periodicity is nocturnal (Manson).

As an explanation of this striking anomaly it has been suggested that the non-periodic microfilaria is the progeny of a parent worm specifically distinct from *F. bancrofti*; but Leiper has failed to find any anatomical difference between the Fijian worm and the *F. bancrofti* of India, China, and S. America. Fülleborn and the Editor, after minute study and comparison of the histology of the microfilariæ from those countries, find that they are identical in every respect. It may be, as the Editor suggested, that the non-periodic

Digitized by Google

habit of the Pacific microfilaria is a partial adaptation to the day habit of the usual intermediary of the parasite in Fiji and other S. Pacific islands—*Stegomyia pseudoscutellaris* (Plate XXIV.).

The subject of filarial periodicity, especially as regards the blood-worms of the Pacific islands, Queensland, and West Africa, requires further study.

The mosquito the intermediary host of Filaria bancrofti.—Should the females of certain species of mosquito * which have fed on the blood of a filaria-infested individual be examined immediately after feeding, the blood contained in the stomach of the insects will be found to harbour large numbers of living microfilariæ. If one of these insects be examined three or four hours after it has similarly fed, it will be found that the blood-corpuscles have in great measure parted with their hæmoglobin, and that the blood plasma, in consequence of this and of dehydration, has become thickened, although not coagulated. If attention be directed to the microfilariæ in the thickened blood, it will be seen that many of them are actively engaged in endeavouring to escape from their sheaths. The diffused hæmoglobin has so thickened the blood plasma that it has become viscid, and holds, as it were, the sheath. This change in the viscosity of the blood seems to prompt the microfilariæ to endeavour to escape from their sheaths. They become restless, as if excited. Alternately retiring towards the tail end and then rushing forward to the head end of the sheath, the imprisoned parasite butts violently against the latter in frantic efforts to escape. After a time the majority succeed in effect-

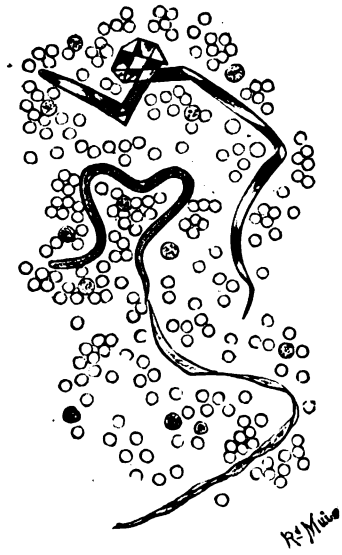
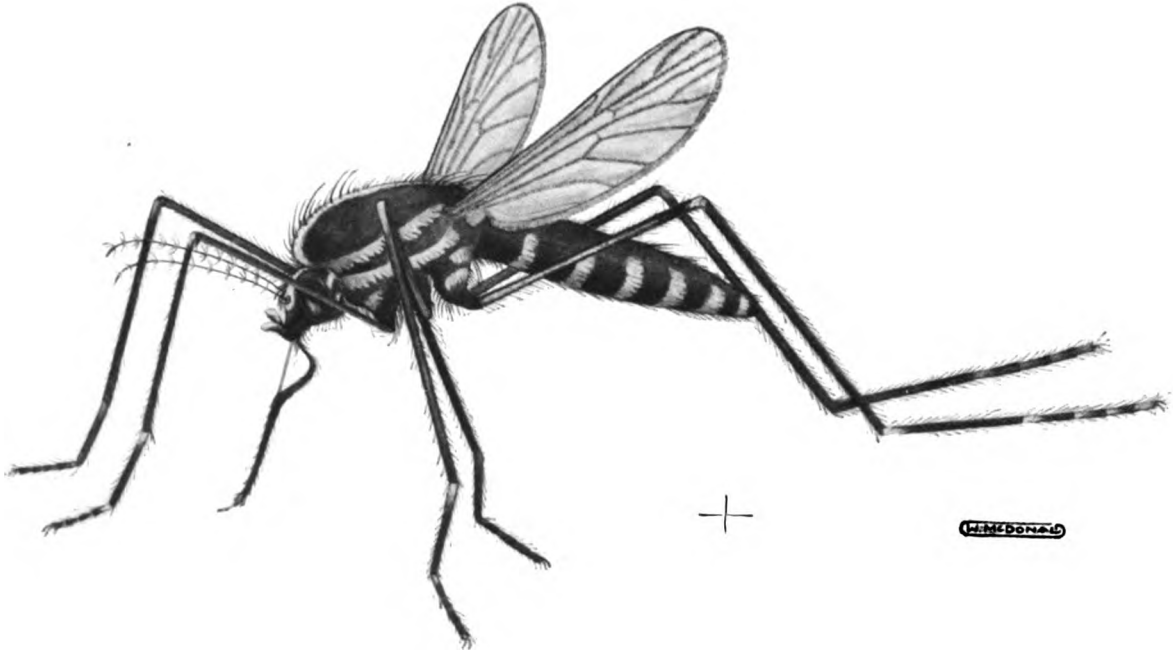


Fig. 143.—Filarial ecdysis.

* Several species may serve as intermediary host. Those so far worked out are *Culex pipiens* in China; *C. fatigans* in the West Indies and the Philippines; *C. quinquefasciatus* in South America; *C. gelidus* and *sitiens* in Malaya, Sumatra, Celebes, and Malacca; *Mansonia uniformis* and *M. annulipes* in Central Africa; *Stegomyia pseudoscutellaris* in Fiji; *S. gracilis*, *S. perplexa*, and *S. scutellaris* in Malaya; *Scutomyia alboline ata* in Malaya; *Taeniorhynchus domesticus* in the same country; *Anopheles rossii* in India; *A. costalis* in West Africa; *A. sinensis*, *A. barbirostris*, and *A. pedilæniatus* in Malaya; *Cellia argyrotarsis* and *C. albipes* in the West Indies.

Digitized by Google



STEGOMYIA PSEUDOSCUTELLARIS, ♀.

PLATE XXIV.

Digitized by Google

Digitized by Google

ing a breach and in wriggling themselves free from the sheaths which had hitherto enclosed them (Fig. 143). This process can be accelerated by chilling the preparations on ice. The microfilaria now swims free in the blood, the character of its movements once more undergoing a remarkable change. Hitherto, though active enough in wriggling about, the parasite did not materially change its position on the slide; but now, having become free, it moves about from place to place—locomotes, in

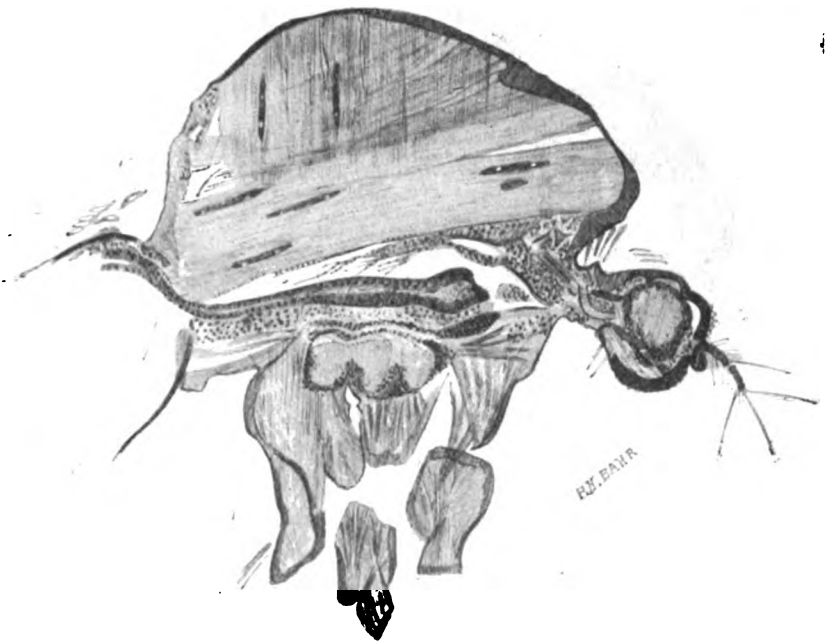


Fig. 144.—Section of thoracic muscles of Stegomyia pseudoscutellaris: second day after feeding on filariated patient. (*Orig.*)

fact. If we dissect a mosquito at a somewhat later period after feeding, it will be found that the stomach of the insect, though still full of blood, contains very few microfilariæ, although their empty sheaths can be seen in abundance. If, however, we break up with needles the thorax of the insect and tease out in normal salt solution the muscular tissue, we shall find that the microfilariæ, after discarding their sheaths, have quitted the stomach and entered the thoracic muscles of the insect, among the fibres of which they are now moving languidly. (Figs. 144, 145.) By a course of serial dissections of filariated mosquitoes we can ascertain

Digitized by Google

that in the thorax of the insect the parasite enters on a metamorphosis which takes from twelve to twenty days (longer or shorter, according to atmospheric temperature) to complete—a metamorphosis eventuating in the formation of a mouth, of an alimentary canal, and of a peculiar trilobed caudal end, as well as in a relatively enormous increase in the size (to $\frac{1}{16}$ in.) and activity of the young parasite. (Figs. 146, 147.) The larval filariæ now quit the thorax.

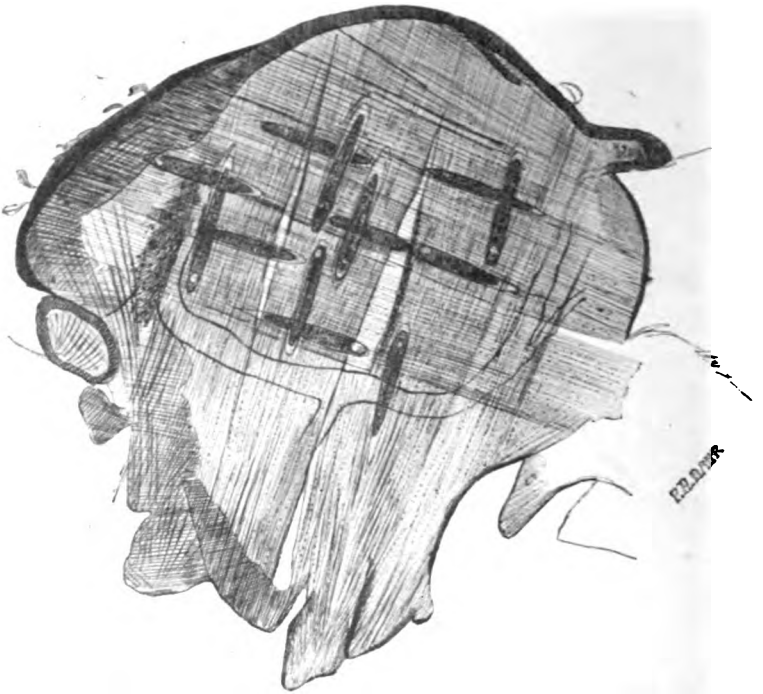


Fig. 145.—Section of thoracic muscles of Stegomyia pseudoscutellaris: fourth day after infestation. (*Orig.*)

A few find their way to the abdomen, where, in properly prepared sections, they may occasionally be seen in the tissues around the stomach, and even among the eggs at the posterior part of the insect. The vast majority pass forwards by the prothorax and neck, and, entering the head, coil themselves up close to the base of the proboscis and beneath the pharynx and under-surface of the cephalic ganglia. Low, in sections prepared at the London School of Tropical Medicine from filariated mosquitoes sent to Manson by Bancroft of Australia, has shown that the filaria in its

Digitized by Google

future progress finds its way into the proboscis; an observation which has been confirmed by James in India, Annett and Dutton in West Africa, by the Editor in Fiji, and by others elsewhere. As

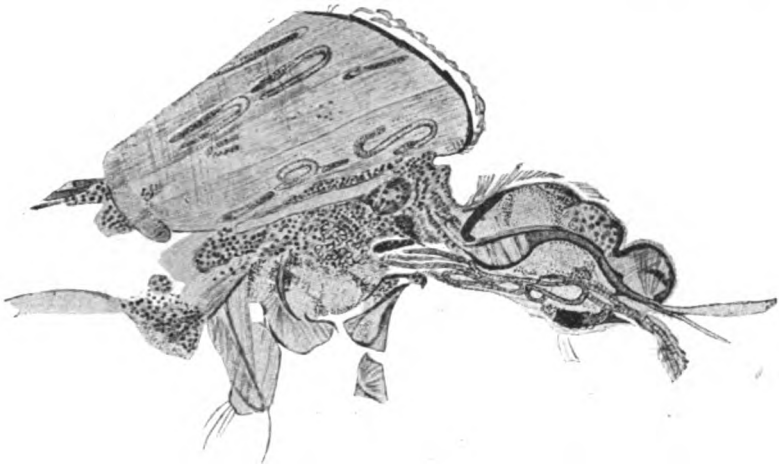


Fig. 146.—Section of Stegomyia pseudoscutellaris, showing filariæ in thorax on tenth day of development, travelling forwards into proboscis. (*Orig.*)

pointed out by Grassi, its exact position here is the interior of the labium (Fig. 148, *a*). Apparently the filariæ seek to emerge (for such must be their object in entering the proboscis) in pairs; at all

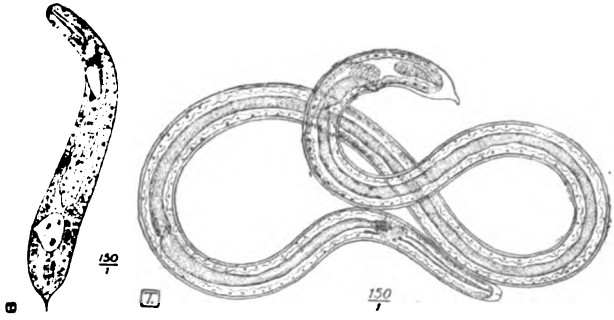


Fig. 147.—Stages of larval form of F. bancrofti, from the thoracic muscles of Culex fatigans. (*After Looss.*)

events, in those sections which the Editor has examined, two worms were in each instance found together, their heads abreast of each other and close to the termination of the labium in the labella.

Digitized by Google

As many as eight have been found packed together in this situation.

The parasites remain in this position awaiting an opportunity to enter a warm-blooded vertebrate host when the mosquito next proceeds to feed. This they appear to do by penetrating the thin membrane that unites the labella to the tip of the proboscis, and so pass on to the surface of the skin, which they penetrate in the neighbourhood of the puncture made by the mosquito (Fülleborn for *Diro-*

Fig. 148.—F. bancrofti in head and proboscis of mosquito. (*G. C. Low.*)
a, *a*, *a*, Filariæ; *b*, labium; *c*, labrum; *d*, base of hypopharynx; *e*, duct of veneno-salivary gland; *f*, *f*, cephalic ganglia; *g*, *g*, eye; *h*, œsophagus; *i*, pharyngeal muscle.

filaria immitis, the Editor for *Filaria bancrofti*) (Figs. 149, 150); they do not enter through the mosquito-made wound, as formerly conjectured, but near to it. Annett and Dutton pointed out that there is a weak point in the chitinous skeleton of the labium of the mosquito just where the labella are jointed on, and that it is at this weak point that the parasites escape. Bancroft confirmed this suggestion by showing that the filariæ enclosed within the labium can readily escape at this point under the least pressure, such as occurs in the buckling of the sheath during haustellation. The filariæ invariably die when extruded at the seat of the bend of the

Digitized by Google

labium. Finally, Lebredo and the Editor, by placing living infested mosquitoes on slides and irrigating with warm saline solution, proved that the filariæ escape from the extreme tip of the proboscis. Larval filariæ have been observed to escape within a minute. A temperature too high kills both larvæ and mosquito; one too low arrests development. Sometimes the larval filaria in its progress through the thorax becomes arrested and dies. The defunct worm then becomes enclosed, like a mummy, in a case of chitin inside the mosquito's body, resulting in the curious structure

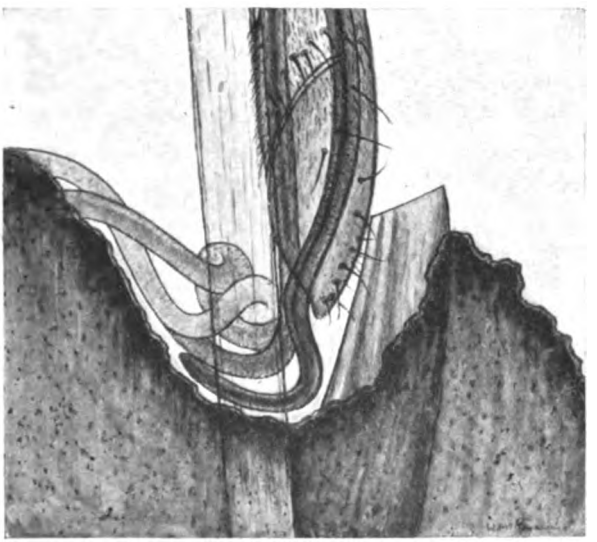


Fig. 149.—Larval filariæ (Dirofilaria immitis) leaving proboscis of mosquito and burrowing through the skin. (*Partly diagrammatic, after Fülleborn.*)

represented in Fig. 151. The process is possibly allied to the calcification of the adult worm in the human body. Apparently the filariæ in some instances can discriminate between flesh and vegetable, for in mosquitoes fed on bananas the parasites had not been deceived into passing into so inhospitable a medium; up to forty days after the insect was infected, and after many meals of banana, they could still be found coiled up in the head or stretched out in the labium. Probably heat and moisture play a part in this respect, as has been shown to be the case by Fülleborn.

These observations prove that, like the malaria parasite, the

Digitized by Google

filaria is introduced into its human definitive host by mosquito bite. Whether it may obtain an entrance by any other channel or medium it would be hard to prove and rash to deny. That the young mosquito-reared filaria can live in water for a time (about seven hours) is certain. It is conceivable that some of them, such as those which, at the completion of their stage of development in the mosquito, find their way into the abdomen of the insect, may escape into water when the mosquito lays her eggs or dies, and so obtain access to the skin of man.

Once introduced into the human body, the filaria finds its

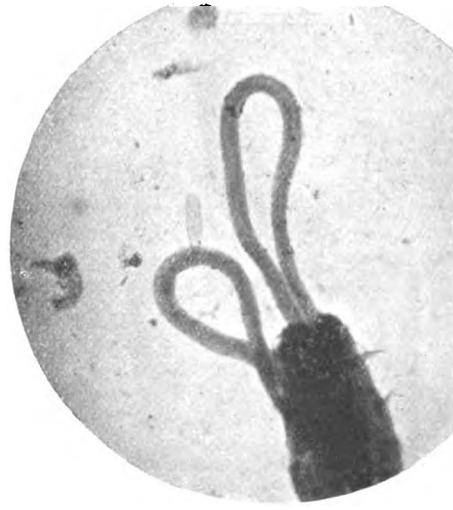


Fig. 150.—Two filariæ emerging from proboscis of Stegomyia pseudoscutellaris. (*Orig.*)

way into the lymphatics and glands. Arrived in one of these, it attains sexual maturity; possibly after a period of six months or more fecundation is effected, and in due course new generations of larval filariæ are poured into the lymph. These, passing through the glands—if such should intervene—by way of the thoracic duct and left subclavian vein, or by the lymphatics of the upper part of the body, finally enter the circulation.

Such is the life-history of *Filaria bancrofti;* man is its definitive host, the mosquito its intermediary host. It is manifest that filarial periodicity is an adaptation of the habits of the parasite to the nocturnal habits of the mosquito. It is also manifest

Digitized by Google

that the purpose of the "sheath" with which it is provided while circulating in the human host is to muzzle the young filaria and prevent its breaking through the blood-vessels, thereby missing

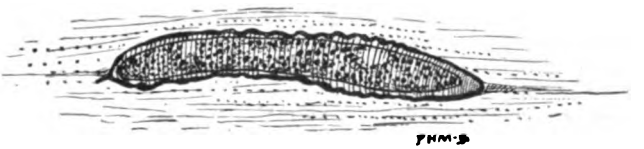


Fig. 151.—Chitinized filaria in thorax of mosquito. (*Orig. preparation.*)

its chance of gaining access to the mosquito. The cephalic armature is adapted for piercing the walls of the mosquito's stomach, and for enabling the parasite to travel through the tissues of the insect.

Parental forms.—The parent filariæ have been found many times. They are long, hair-like, transparent nematodes, 3–4 in. in length (Fig. 152). The sexes live together, often inextricably coiled about each other. Sometimes they are enclosed, coiled up several in a bunch and tightly packed, in little cyst-like dilatations of the distal lymphatics (Maitland); sometimes they lie more loosely in lymphatic varices; sometimes they inhabit the larger lymphatic trunks between the glands, the lymphatic glands themselves, and, probably not infrequently, the thoracic duct.

The *female filaria* is the larger, both as regards length and thickness; she

Fig. 152.—F. bancrofti (natural size): *a*, male; *b*, female.

measures 65–100 mm. in length by 0·20–0·28 mm. in breadth. The two uterine tubes, occupying the greater extent of her body, are filled with ova at various stages of development. In both sexes the oral end, armed with a double row (number uncertain) of exceedingly minute papillæ, is slightly tapered, club-shaped and simple; the tail also is tapered to comparatively small dimensions, its tip being rounded off abruptly. The vagina opens on the ventral surface about 0·6–1·3 mm. from the anterior extremity; the anus just in advance of the tip of the tail. The cuticle is smooth and without markings.

To the naked eye the *male worm* is characterized by its slender dimensions (about 40 mm. in length by 0·1 mm. in diameter), by its marked disposition to curl, and by the peculiar vine-tendril-like tail, the extreme end of which is sharply incurvated (Fig. 152, *a*). The cloaca gives exit to two slender, unequal spicules (0·2 and 0·6 mm. respectively). The existence of caudal papillæ in the male worm has been ascertained by Leiper. There are in all two rows of fifteen each, of which four are preanal, and extremely minute.

The life-spans of *F. bancrofti* and its microfilaria have not been determined. From the fact that the microfilariæ have been found in the blood many years

Digitized by Google

after the opportunity of infection has passed, it is to be concluded that both of them may live for many years. Experiments with the microfilaria of the dog—*Filaria* (*Dirofilaria*) *immitis*—have shown that in the case of this worm the microfilaria may live for at least three years, and in this time acquire somewhat increased dimensions, but it does not follow that such is the case with *microfilaria bancrofti*. The latter has been seen to disappear completely from the circulation within a few hours of the death of the parent worms during an attack of lymphangitis. Nothing is known of what becomes of the microfilariæ when they grow effete or die.

As shown by Wise and the Editor, the mature worm is cretified after its death, and may be found, sometimes in large numbers, in this condition in the lymphatic vessels and glands. (Figs. 153, 154, 155.)

Fig. 153.—Calcified F. bancrofti lying in and blocking a lymphatic vessel. (*Orig.*)

Age- and sex-incidence.—In most countries in which filariasis is common it appears to be the rule that the incidence of infestation is greatest in the male sex, though, in British Guiana, Daniels and Conyers reported twice as many females infested as males. This exception to the general rule probably finds an explanation in the habits of the natives. The Editor's statistics from Fiji show that of 1,320 people of Fijian blood, 30·4 per cent. of males and 23·9 per cent. of females were filariated. The incidence is greatest in both sexes after the twentieth year (this is true for the Pacific islands, as well as for China according to Manson and Duncan Whyte); comparatively more females than males are infested below the age of 10. The youngest infested subject in the Editor's experience was a Fijian girl of about 5. Croll's statistics from Brisbane show that out of 4,000 Europeans admitted to hospital during 1909–10, 11·5 per cent. had microfilariæ, and of these 5 per cent. were

Digitized by Google

children under 12. The rate of filariation varies considerably in different islands of the Pacific, and even in different districts of the same island, and is in direct proportion to the incidence of elephantiasis and other filarial diseases. In an investigation conducted in 1912 in Ceylon the Editor found that, whereas 26 per cent. of the adults of some of the villages were infested, in neighbouring ones the inhabitants were quite free from the parasite and its associated diseases. This apparent anomaly requires further investigation.

Morbid anatomy and pathology. *The filaria not generally pathogenic.*—In most cases of filarial infection the parasite exercises no manifest injurious influence whatever. In a certain

Fig. 154.—Section of a fibrosed lymphatic gland. (*Orig.*)
A, Portions of a calcified *F. bancrofti*; B, partially occluded lymphatic vessel.

proportion of instances, however, there can be no doubt that it does have a very prejudicial effect on its host, and this mainly by obstructing lymphatics. The healthy, fully formed microfilariæ—that is to say, the larval filariæ which, by means of the microscope, we see in the blood—have, so far as we can tell, no pathogenic properties whatever. It is otherwise as regards the parent worm, the toxins which it excretes, and, perhaps, its prematurely extruded ova.

Filarial disease originating in injury of lymphatic systems.—Roughly speaking, the filaria causes two types of disease: one characterized by varicosity of lymphatics, the other by more or

Digitized by Google

less solid œdema. The exact way in which the parasite operates has not been definitely and absolutely ascertained for all types of filarial disease. Apparently, in some instances, a single worm, or a bunch of worms, may plug the thoracic duct, and act as an embolus or originate a thrombus; or, the worm may give rise

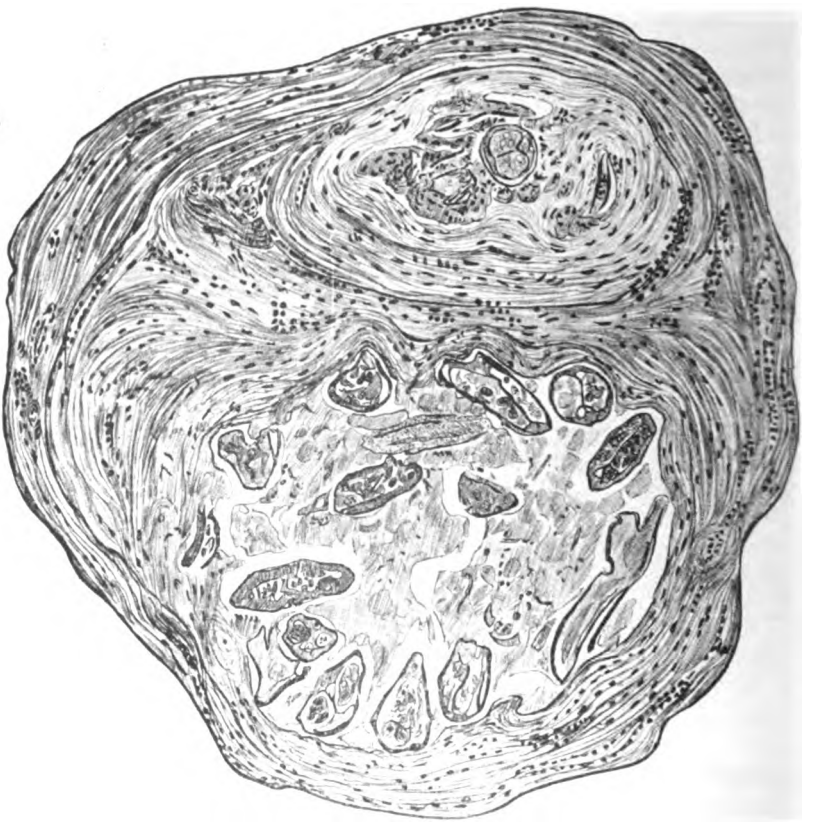


Fig. 155.—Section of a thickened brachial lymphatic containing portions of dead filariæ undergoing disintegration and blocking the lumen of the vessel. Note the large amount of fibrosis. (*Orig.*)

to inflammatory thickening of the walls of this vessel, and so lead to obstruction from the consequent stenosis or thrombosis. In other instances the minor lymphatic trunks and the glands may be similarly occluded. As an effect of either form of occlusion, the lymphatic areas drained by the implicated vessels are cut

Digitized by Google

off from the general circulation, and varicosity or œdema, or both, ensue.

The Editor's work in Fiji has shown that the afferent lymphatic glands situated at some considerable distance from the actual seat of the filaria worms (i.e. the inguinal lymphatics), for instance the lumbar glands, undergo considerable changes, as evidenced by fibrosis, focal necrosis, and giant-cell formation. These changes may be due to the destruction of microfilariæ within the gland substance, or to toxins actually excreted by the adults either while living or subsequently to their death. More work is required on this aspect of the subject.

Pathology of lymphatic varix.—In consequence of the rich anastomosis existing between the contiguous lymphatic areas, on filarial obstruction occurring in one of them a compensatory lymphatic circulation is sooner or later established. But before this can be properly effected a rise of lymph pressure and a dilatation of the lymphatics in the implicated area must take place. This leads to lymphatic varix of different kinds, degrees, and situations. When the seat of filarial obstruction is the thoracic duct, the chyle poured into that vessel can reach the circulation only by a retrograde movement; consequently, this fluid may be forced to traverse in a retrograde way the abdominal and pelvic lymphatics, the lymphatics of the groin, scrotum, and abdominal wall. As a consequence, these vessels, together with the thoracic duct up to the seat of obstruction, become enormously dilated. In dissections of such cases (Fig. 156) the thoracic duct has been found distended to the size of a finger, the abdominal and pelvic lymphatics forming an enormous varix, perhaps a foot in diameter and many inches in thickness, concealing kidneys, bladder, and spermatic cords. In such cases, when one of the vessels of the varix is pricked or ruptures, the contents are found to be white or pinkish. They are not limpid like ordinary lymph. They are chyle, therefore—chyle on its way to enter the circulation by a retrograde compensatory track. When the varix involves the integuments of the scrotum, the result is "lymph scrotum"; when most prominent in the groin, then a condition of glands is produced which Manson called "varicose groin glands"; when the lymphatics of the bladder or kidneys are affected and rupture from over-distension, then chyluria is the result; when those of the tunica vaginalis rupture, then there is chylous dropsy of that sac —"chylocele"; the same may happen in the peritoneum—chylous ascites. Occasionally varicose lymphatic glands, resembling those frequently encountered in the groins, are found

Digitized by Google

in the axilla. Occasionally, also, limited portions of the lymphatic trunks of the limbs are similarly and temporarily, or more permanently, distended. This, doubtless, is the pathology of all those forms of filarial disease characterized by visible varicosity of lymphatics, with or without lymphorrhagia. It may happen that the obstruction is in some lymphatic tract on the distal side of the entrance of the chyle-bearing vessels into the receptaculum chyli. In this case a rupture of the consequent lymphatic varix will give issue to a limpid lymph unmixed with chyle.

Microfilariæ may disappear from the blood in such cases.—

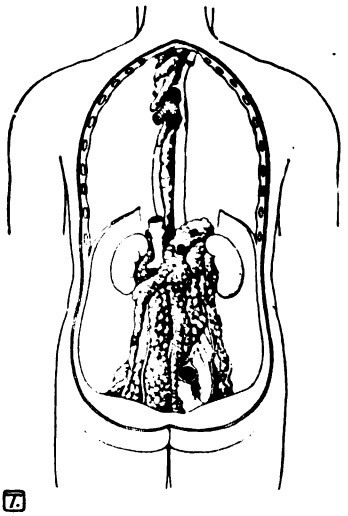


Fig. 156.—Dissection of the lymphatics in a case of chyluria, showing the dilated right and left renal lymphatics and thoracic duct. (*Mackenzie, Trans. Path. Soc. Lond.*)

In filarial disease associated with lymphatic varix, microfilariæ are generally present in the blood as well as in the contents of the dilated vessels. Sometimes, it is true, the microfilariæ are not found. Such cases are probably of long standing; had the microfilariæ been looked for at an earlier stage of the disease, they would presumably have been discovered. Cases in which the microfilariæ have disappeared in this way have been observed by Manson, and later by the Editor. The reason for this disappearance is doubtless the death of the parent parasites, an occurrence generally associated with attacks of acute lymphangitis. Although the original cause of the varix may thus disappear, the effect is permanent.

Digitized by Google

Pathology of elephantiasis arabum. *Microfilariæ are not usually present in the blood in elephantiasis.*—In those cases of filarial disease in which elephantiasis is the leading feature, it is not usual at any stage of the established disease to find microfilariæ in the blood or elsewhere, unless it be in countries in which filariasis is extremely common and re-infection, or extensive infection, highly probable.

Reasons for regarding elephantiasis as a filarial disease.—From this circumstance—the absence of microfilariæ from the blood in elephantiasis—the question naturally arises, Why attribute this disease to the filaria? The answer to this is: (1) The geographical distribution of *Filaria bancrofti* and of elephantiasis arabum corresponds; where elephantiasis abounds there the filaria abounds, and vice versa. (2) Filarial lymphatic varix and elephantiasis occur in the same districts, and frequently concur in the same individual. (3) Lymph scrotum, an unquestionably filarial disease, often terminates in elephantiasis of the scrotum. (4) Elephantiasis of the leg sometimes supervenes on the surgical removal of a lymph scrotum. (5) Elephantiasis and lymphatic varix are essentially diseases of the lymphatics. (6) Filarial lymphatic varix and true elephantiasis are both accompanied by the same type of recurring lymphangitis. (7) As filarial lymphatic varix is practically proved to be caused by the filaria, the inference appears to be warranted that the elephantiasis of warm climates, with rare exceptions—the disease with which the former is so often associated and has so many affinities—is attributable to the same cause.

Explanation of the absence of microfilariæ from the blood in elephantiasis.—If the filaria be the cause of tropical elephantiasis, how account for the absence of the embryos from the blood, as is the case in the majority of instances of this disease? The answer is: Either the disease-producing filariæ have died; or the lymphatics draining the affected area are so effectually obstructed by the filaria, its products, or its effects, that any microfilariæ they may contain, or may have contained, cannot pass along these vessels to enter the circulation. Adult filariæ of both sexes in large numbers may be found in enlarged fibrosed lymphatic glands —epitrochlear, for example—without the presence of microfilariæ in the bloodstream.

We have already said that in filarial lymphatic varix the parasites which produced the disease may die, particularly during attacks of lymphangitis; we have also seen that they may become cretified and may be found in large numbers in this condition or

Digitized by Google

alive in the glands and lymphatic trunks, where, as the Editor has shown, they give rise to giant-cell formation and fibrotic changes of an obstructive nature. (Fig. 154.) This may not, however, be the entire explanation of the origin of tropical elephantiasis. At times filarial ova, possibly the products of abortion by the female worms, have been found by Manson, and more recently by the Editor, in the lymph procured by aspiration of a varicose groin-gland. Manson believed that these ova, being of considerably larger diameter than the long, slim, and active microfilaria, cause an obstruction of the finer lymphatics by embolism. On the other hand, observations on the actual contents of filariated glands suggest that these ova are derived from disintegrating dead parent worms.

It is the Editor's belief that the real origin of obstruction is the fibrotic changes in the lymphatic vessels and lymph-glands in most cases.

Inflammation necessary for the production of tropical elephantiasis.—Lymph stasis alone does not produce elephantiasis; this has been proved by experimental ligature of lymphatic trunks. It may produce a form of œdema, but not true elephantoid hypertrophy. Should inflammation occur in an area of lymphatic congestion so produced, as it is very apt to do on the slightest injury, then elephantiasis will supervene; for, unless the lymphatics of an inflamed area are patent, the products of inflammation are not completely absorbed. Erysipelatoid inflammation, frequently recurring, is a well-recognized feature of almost every case of elephantiasis arabum.

Sequence of events in elephantiasis.—The sequence of events in the production of elephantiasis, Manson believes, is as follows: Parent female filaria in the lymphatic system of the affected part; obstructive fibrotic changes in the glands or lymphatic trunks—or, injury of the filaria leading to premature expulsion of ova; impermeability of lymphatic glands supervening on either of these causes of obstruction; stasis of lymph; lymphangitis due to bacterial invasion through wounds of the skin, or to toxins derived from the parent worm itself, or to the products of disintegration of the microfilariæ in the congested area; imperfect absorption of the products of inflammation; recurring attacks of inflammation from similar causes leading to gradual, intermittently progressive, inflammatory hypertrophy of the part.

In this way one can explain the production of elephantiasis by the filaria, and the absence from the blood of the embryos of the parasite which started the disease; the latter cannot pass

Digitized by Google

the occluded glands. Very likely the parent worm or worms die at an early stage of the disease, killed by the subsequent lymphangitis, or by the cause which led to premature parturition. The lymph aspirated from the inflamed area has proved, in the Editor's experience, sterile on culture, though Leber and others regard a diplococcus, or a streptococcus, as being the excitant.

That lymphangitis is not a necessary precursor of *all* cases of elephantiasis may be gathered from a study of elephantiasis of the extremities in temperate climates. Of these a proportion may be ascribed to an inflammation of septic origin affecting the main lymphatic trunks, while others, albeit somewhat rare, supervene without any ascertainable exciting cause.

The subjects of elephantiasis less liable than others to microfilariæ in the blood.—Many years ago Manson made a curious observation which supports the view just stated. In examining slides of night blood from 88 natives of Cochin, of whom 14 were affected with elephantiasis, he found that 74 were not so affected. Of the slides coming from the 74 non-elephantiasis cases, 20 contained microfilariæ, one in every 3½; of the 14 elephantiasis cases, only 1 had microfilariæ. Why should the elephantiasis cases have proportionately fewer microfilariæ than the non-elephantiasis cases? The answer may be that in the former the existence of elephantiasis implied that a large area of their lymphatic systems was blocked, and the blood could be stocked with microfilariæ carried by the lymph from only a relatively small lymphatic area; and that there was therefore a proportionately lesser likelihood of the presence of parent filariæ having for their young an unobstructed passage to the blood.

This apparent anomaly exists in other filarial diseases as well. In Fiji, for instance, the Editor found the microfilaria-rate for cases of elephantiasis to be 38·2 per cent., while the microfilaria-rate in cases of glandular enlargement, also of filarial origin, was 34·6 per cent. In examining all those with clinical manifestations of filarial disease amongst the Fijians, it was found that 19·7 per cent. of males and only 6·3 per cent. of females thus affected had embryos present in the bloodstream, and moreover that no less than 44·8 per cent. of those with microfilaria demonstrable in the bloodstream showed no obvious signs of disease at all.

Filarial Diseases

Enumeration of the filarial diseases.—The diseases known to be produced by *F. bancrofti* are abscess; lymphangitis; arthritis; synovitis; abscess of hip-joint; varicose groin-glands; varicose

Digitized by Google

axillary glands; lymph scrotum; cutaneous and deep lymphatic varix; orchitis; funiculitis; chyluria; elephantiasis of the leg, scrotum, vulva, arm, mamma, and elsewhere; chylous dropsy of the tunica vaginalis; chylous ascites; chylous diarrhœa, and probably other forms of disease depending on obstruction or varicosity of the lymphatics, or on the death of the parent filariæ, including peritonitis and secondary infections by pyogenic micro-organisms.

Abscess.—Occasionally, as already mentioned, whether in consequence of blows or other injuries, of lymphangitis, or of unknown causes, the parent filariæ die. Generally the dead body is absorbed, just as a piece of aseptic catgut would be, or becomes cretified.* Sometimes the dead worm acts as an irritant and causes abscess, in the contents of which fragments of the filaria may be found. Such abscesses, occurring in the limbs or scrotum, will discharge in due course, or may be opened; if properly treated surgically they may lead to no further trouble. Should they form in the thorax or abdomen, serious consequences and even death may ensue. From personal observations in these cases it was found to be due to the fortuitous supervention of a pyogenic infection that these abscesses developed; the starting-point would appear to be a hæmorrhage in the immediate vicinity of the worm. When no such occurrence takes place the defunct filaria becomes cretified.

Probably, in certain instances, abscess forms at times independently of the death of the parasite; e.g. in varicose glands, in lymph scrotum, in elephantiasis.

The death of the parent filaria is apt to be lost sight of as a possible cause of abscess in the subjects of filarial infection. Deep-seated pain in the thorax or abdomen, with inflammatory fever followed by hectic, and a diminution in the number of microfilariæ in, or their entire disappearance from, the peripheral blood, should in such circumstances suggest a diagnosis of filarial abscess and indicate exploration and, if feasible, active surgical interference. Should the condition not be readily recognized, a fatal staphylococcal or streptococcal septicæmia may supervene.

Lymphangitis and elephantoid fever. *Symptoms.*—Lymphangitis is a common occurrence in all forms of filarial disease, particularly in elephantiasis, varicose glands, and lymph scrotum.

* Wise and Minett have found filariæ, living or cretified, in the following situations, viz.: pelvis of kidney (31 times), epididymis (18 times), retroperitoneum (12 times), the ilio-psoas muscle (4 times), Glisson's capsule (twice), inguinal glands (25 times), lymphatic vessels (8 times). Similar observations have been made by the Editor in Fiji.

Digitized by Google

When occurring in the limbs the characteristic painful, cord-like swelling of the lymphatic trunks and associated glands, and the red congested streak in the superjacent skin, are usually apparent at the commencement of the attack. Very soon, however, the connective tissue and skin of the implicated area become inflamed and tense, and high fever, preceded by a severe and prolonged rigor, sets in. The attack may continue for several days, and be accompanied by severe headache, anorexia, often vomiting, and sometimes delirium. After a time the tension of the inflamed integuments may relieve itself by a lymphous discharge from the surface. Usually the attack ends in profuse general diaphoresis. The swelling then subsides gradually though not entirely. Lymphangitis may be confined to groin glands, testis, spermatic cord, or abdominal lymphatics. When it affects an extensive abdominal varix, symptoms of peritonitis are rapidly developed and may prove fatal. The lymph aspirated from the inflamed lymphatic trunks proved in the Editor's experience to be sterile ; the reaction is possibly due to toxins given off by the adult parasite or its embryos in the process of disintegration.

Filarial fever without any external signs.—In Fiji a form of filarial fever is common in heavily infested districts without any obvious lymphangitis ; this is probably due to inflammation of the deep-seated lumbar lymphatics or glands.

Diagnosis.—This fever, appropriately named by Fayrer "elephantoid fever," occurs habitually at varying intervals of weeks, months, or years, in nearly all forms of elephantoid disease. Its tendency to recur, the severe rigor ushering it in, and the terminal diaphoresis cause it to be mistaken for ague. In Barbadoes, where there is no malaria, it is habitually called "ague." Among the Fijians it is known as "wanganga" and in Samoa as "mumu fever." The implication of the lymphatics, the local pain, the erysipelatoid redness and swelling, the prolonged pyrexial stage, the absence of the malaria parasite from the blood, the presence there very possibly of microfilariæ, and the powerlessness of quinine to control the fever, suffice for diagnosis. Nevertheless, error in diagnosis is common, particularly when the attacks recur frequently and with a certain degree of regularity, as is usually the case.

Treatment.—The treatment should consist in removing any cause of irritation, in rest, elevation of the affected part, cooling lotions or warm fomentations, mild aperients, opium or morphia to relieve pain, and, if tension is great, pricking or scarifying the swollen area under suitable aseptic conditions. Subsequently

Digitized by Google

the parts, if their position permits, should be elevated and firmly bandaged.

Varicose groin-glands.—(Figs. 157, 158).—Varicose groin-glands are frequently associated with lymph scrotum, with chylous dropsy of the tunica vaginalis, or with chyluria. Occasionally all four conditions coexist in the same individual.

Symptoms.—As a rule the patient is not aware of the existence of these varicose glands until they have attained considerable dimensions. Then, a sense of tension, or an attack of lymphangitis,

Fig. 157.—Varicose groin-glands and chylocele.

calls attention to the state of the groins, where certain soft swellings are discovered. These swellings may be of insignificant dimensions or they may attain the size of a fist. They may involve both groins, or only one groin; they may affect the inguinal glands alone, or the femoral glands alone, or (and this is generally the case) both sets together.

To the touch they feel soft, doughy, and obscurely lobulated. The skin, natural in appearance, can be glided over the surface, but the swellings themselves are not movable over the subjacent fascia. Occasionally hard, kernel-like pieces can be felt in their interior, or the entire mass may be more or less indurated. On

Digitized by Google

thrusting a hypodermic needle into the swellings, white or reddish chylous or clear lymphous fluid can be aspirated, sometimes in great abundance. This fluid coagulates rapidly, and usually contains living microfilariæ or filarial ova.

Diagnosis.—It is important to be able to diagnose these tumours from hernia, for which they are often mistaken. This can be done by observing that they are not tympanitic on percussion; that though pressure causes them to diminish, they do so slowly; that there is no sudden dispersion accompanied by gurgling, as in hernia, on taxis being employed; that they convey a rela-

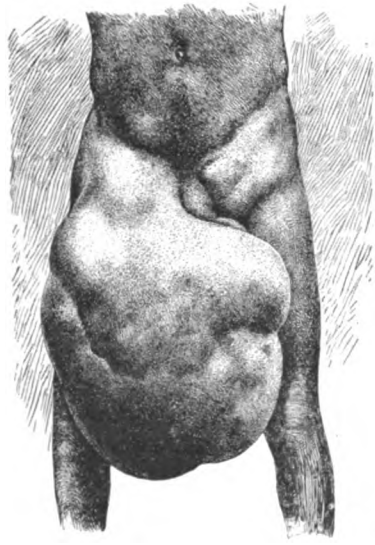


Fig. 158.—Unusually large varicose groin-glands.
("*Journ. of Trop. Med.*")

tively slight or no impulse on coughing; that they slowly subside on the patient lying down, and slowly return, even if pressure be applied over the saphenous or inguinal openings, on the erect posture being resumed. The cautious use of the hypodermic needle will confirm diagnosis, which would be further strengthened by the coexistence of lymph scrotum, chyluria, or chylous hydrocele, and the presence of filariæ in the blood. *Chronic swellings about the groin, cords, testes, and scrotum in patients from the tropics should always be regarded as possibly filarial.*

Pathological anatomy.—On dissection these tumours are found to consist of bunches of varicose lymphatics, and, it may be,

Digitized by Google

to form part of a vast lymphatic varix involving the pelvic and abdominal lymphatics.

Treatment.—Unless they give rise to an incapacitating amount of discomfort, and are the seat of frequent attacks of lymphangitis, varicose groin-glands are best left alone. It must always be remembered that they are part of an anastomosis—it may be necessary to life. Should they be very troublesome and incapacitate for work, they may be removed. In operating, strict aseptic methods must be practised, as septic lymphangitis readily occurs and has frequently proved fatal after operations in such cases. Excision is not always satisfactory, as it may be followed by lymphorrhagia at the seat of the wound, by excessive dilatation of some other part of the implicated lymphatic area, by chyluria, or by elephantiasis in one or both legs.

Manson has suggested that these tumours might be treated by establishing an anastomosis between one of the dilated lymphatic vessels and a neighbouring vein. Sir Rickman Godlee has twice performed such an operation with partial success: it is somewhat difficult, owing to the fragile nature of the dilated lymphatic vessels and the shortness of their course.

Similar varicose dilatation of the axillary glands is sometimes, though much more rarely, found. Bancroft designated these varicose axillary and groin glands "helminthoma elastica."

Cutaneous and deeper lymphatic varices.—Occasionally cutaneous lymphatic varices are seen on the surface of the abdomen, on the legs, arms, and probably elsewhere. Sometimes they are permanent; sometimes, when more deeply situated, they constitute little swellings which come and go in a few hours; it may be that the latter often depend on the actual presence of parent filariæ in the tumour, causing lymphatic obstruction. Filarial lymphangiectasis of the spermatic cord is not uncommon. The contents may be milky and chylous, or straw-coloured and lymphous, according to situation and connections.

Thickened lymphatic trunks.—In cases of lymphangitis, after the initial swelling and inflammation have subsided, a line of thickening remains. On excising this thickened tissue and carefully dissecting it, minute cyst-like dilatations of the lymphatic involved have been found by Maitland, Daniels, and the Editor, and in these cysts, coiled up, adult filariæ, sometimes dead, sometimes alive. Manson related that once on the subsidence of a filarial lymphangitis of the arm a thickening, about the size of a finger-tip, remained on the forearm. Believing that it contained adult

Digitized by Google

filariæ, he had this thickening excised and placed in normal salt solution. Eight hours later the mass was carefully dissected, and a living female filaria, about 4 in. in length, was turned out. The parasite continued to live and swim about actively in the salt solution for nearly two hours.

Filarial glandular enlargement.—In the Pacific islands great enlargement of the lymphatic glands with fibrotic changes is by far the most frequent symptom of filarial disease. The epitrochlear gland, for instance, is often affected—in Fiji in 22 per cent. of the total population.

The groin-glands are often very much enlarged, sometimes to 2 or 3 in. across, and may form permanent tumours in the groin. On section they have the appearance of an unripe pear, the central portion being fibrotic, and the peripheral glandular. The deep-seated glands—the iliac, lumbar, mesenteric, and mediastinal—may also be enlarged.

On careful dissection live filariæ or their calcified remains may be demonstrated in the glandular substance. (Fig. 159.)

Treatment.—It is inadvisable to remove these glands surgically, seeing that, as in the case of varicose groin-glands, an incurable lymphocele may result.

Lymph scrotum. (Fig. 160.) *Symptoms.*—In this disease the scrotum is more or less enlarged. Though usually silky to the touch, on inspection the skin presents a few, or a large number of, smaller or larger lymphatic varices which, when pricked or when they rupture spontaneously, discharge large quantities of milky, or sanguineous-looking, or straw-coloured, rapidly coagulating lymph or chyle. In some cases 8 or 10 oz. of this substance will escape from a puncture in the course of an hour or two; it may go on running for many hours on end, soiling the clothes of the patient and exhausting him. Usually microfilariæ can be discovered in the lymph so obtained, as well as in the blood of the patient. In a large proportion of cases of lymph scrotum the inguinal and femoral glands, either on one or on both sides, are varicose.

Probably provoked by friction against the thighs and clothes, erysipelatoid inflammation and elephantoid fever are frequent occurrences. Abscess is not uncommon. In time, in a proportion of cases, the scrotum tends to become permanently thickened and to pass into a state of true elephantiasis.

Treatment.—Unless inflammation be a frequent occurrence, or there be frequent and debilitating lymphorrhagia, or unless the disease tend to pass into true elephantiasis, lymph scrotum

Digitized by Google

—kept scrupulously clean, powdered, suspended, and protected —had better be left alone. Should, however, for these or other reasons, it be deemed expedient to remove the diseased tissues, this can be effected easily. The scrotum should be well dragged down by an assistant whilst the testes are pushed up out of the way of injury. A finger knife is then passed through the scrotum, and

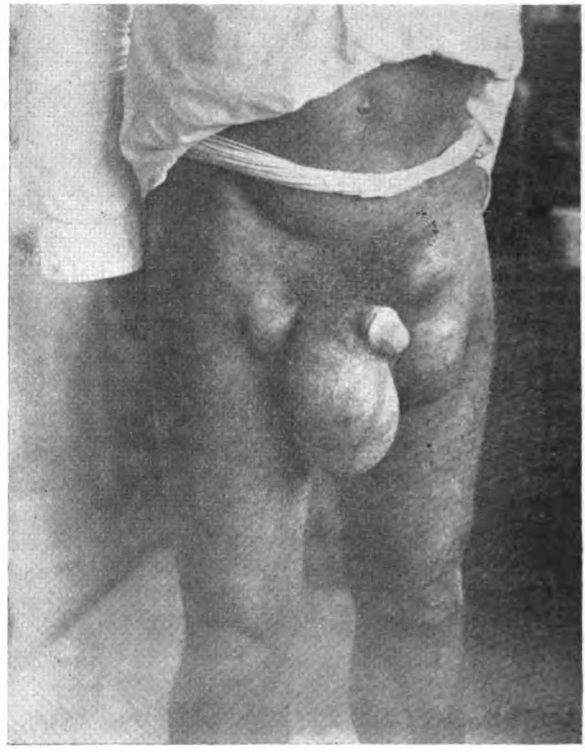


Fig. 159.—Pedunculated groin-glands in a Fijian with double hydrocele. (*Orig.*)

These glands, containing adult ♂ and ♀ filariæ, were removed at operation. No microfilariæ were found in the blood. There were also masses of enlarged glands in right groin.

in sound tissues, just clear of the testes, and the mass excised by cutting backwards and forwards. No diseased tissues, and hardly any flap, should be left. Sufficient covering for the testes can be got by dragging on and, if necessary, dissecting up the skin of the thighs, which readily yields and affords ample covering. It is a very common but a very great mistake to remove too little.

Digitized by Google

As a rule, the wound, if carefully stitched and dressed antiseptically, heals rapidly.

In consequence of this violent interference with a large varix, of which that in the scrotum is but a part, chyluria, or elephantiasis of a leg, may supervene. The patient should be warned of this possibility.

Chyluria. *Pathology.*—When a lymphatic varix in the walls of

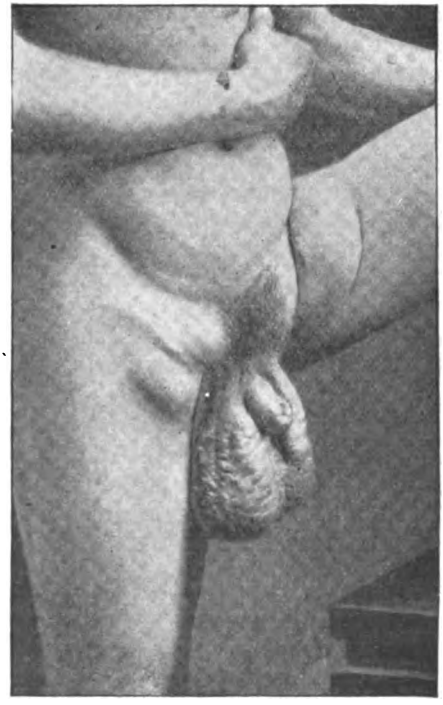


Fig. 160.—Lymph scrotum and varicose groin-glands.
(Photo: Dr. Rennie, Foochow.)

the bladder, or elsewhere in the urinary tract, the consequence of filarial obstruction in the thoracic duct or in the lymphatics of the urinary system, ruptures, there is an escape of the contents of the lymphatics into the urine. Chyluria, or lymphuria, is the result. Low, who was able to investigate a case of lymphuria shortly after death, found that in this instance the lymphatic obstruction was located in the kidney lymphatics themselves, and was due to calcified adult filariæ.

Digitized by Google

A curious fact about this form of filarial disease is that in the Pacific islands it is practically unknown, though it is frequently met with in filariated subjects in India, China, and North Africa.

Symptoms.—This disease frequently appears without warning; usually, however, pain in the back and aching sensations about the pelvis and groins—probably caused by great distension of the pre-existing lymphatic varix—precede it. Retention of urine, from the presence of chylous or lymphous coagula, is sometimes the first indication of serious trouble. Whether preceded by aching, or by retention, or by other symptoms, the patient becomes suddenly aware that he is passing milky urine. Sometimes, instead of being white, the urine is pinkish or even red; sometimes white in the morning, it is reddish in the evening, or vice versa. Sometimes, whilst chylous at one part of the day, it is perfectly limpid at another. Great variety in this respect exists in different cases, and even in the same case from time to time, depending on temporary closure of the rupture in the lymphatic, and also on the nature of the food.*

Physical characters of chylous urine.—If chylous urine be passed into a urine glass and allowed to stand, as a rule, within a very short time, the whole of the urine becomes coagulated. Gradually the coagulum contracts until, at the end of some hours, a small, more or less globular clot, usually bright red or pinkish in colour, is floating about in a milky fluid, the appearance of which is entirely due to fat. Later, the milky fluid separates into three layers. On the top there is formed a cream-like pellicle; at the bottom a scanty reddish sediment, sometimes including minute red clots; in the centre the mass of the urine forms a thick, intermediate stratum, milky white or reddish white in colour, in which floats the contracted coagulum. If a little of the sediment be taken up with a pipette and examined with the microscope, it is found to contain red blood-corpuscles, lymphocytes, granular fatty matter, epithelium, and urinary salts, and mixed with these in a large proportion of cases, though not in all, microfilariæ. The middle layer contains much granular fatty matter; whilst the upper, cream-like layer consists of the same fatty material in greater abundance, the granules tending to aggregate into larger oil globules. If a little of the coagulum be teased out, pressed between

* The sanguineous appearance so frequently seen in chylous urine and in other forms of filarial lymphorrhagia possibly depends in some instances on the formation of blood-corpuscles in lymph long retained in the varicose vessels, and as a result of the normal evolution of the formed elements in that fluid; in other instances it is probably caused by rupture of small blood-vessels into the dilated lymphatics.

Digitized by Google

two slides, and examined with the microscope, microfilariæ, more or less active, may be found in the meshes of the fibrin. According to Yorke and Blacklock, the number of microfilariæ in chylous urine varies greatly within the twenty-four hours in quite an irregular manner. If ether or xylol be shaken up with the milky urine, the fat particles are dissolved out and the urine becomes clear; the fat may be recovered by decanting and evaporating the ether which floats on the urine. Boiling the urine throws down a considerable precipitate of albumen. When the urine contains only lymph, fatty elements are absent, or are present in but very small amount. According to Young, a twenty-four-hour sample of chylous urine contains 1·8–2·6 per cent. of fat. The amount of this substance excreted is generally, though perhaps not invariably, dependent on the amount ingested with the diet.

Recovery and relapse.—Chyluria comes and goes in a very capricious manner. Sometimes the urine remains steadily chylous for weeks and months, and then suddenly, without obvious cause, becomes limpid and natural-looking, and free from fat or albumen. Later a relapse will occur, again to disappear after an uncertain time; and so on during a long course of years.

Retention of urine.—Retention of urine is not an unusual occurrence; it is produced by the formation of coagulum in the bladder. The retention usually gives way after a few hours of distress, worm-like clots being passed.

Constitutional effects.—Although chyluria is not directly dangerous to life, yet, being prolonged, it gives rise to pronounced anæmia, with depression of spirits and feelings of weakness and debility, and tends to incapacitate the patient for active, vigorous life.

Exciting causes of chyluria.—Chyluria is very liable to occur, either for the first time or as a relapse, in pregnancy or after childbirth; the disturbance of the pelvic lymphatics in pregnancy and the muscular efforts attending labour apparently causing rupture of pelvic lymphatics previously rendered varicose by filarial obstruction of the thoracic duct. In men, running, leaping, and violent efforts generally are sometimes assigned as its cause; usually the exciting cause is not discoverable.

Lymphuria.—It would be more correct to describe a certain proportion of filarial cases passing cloudy urine as "filarial lymphuria," as Low and Wise have suggested. In these cases the abnormal element is lymph and contains no trace of fat. Albumen is present in considerable quantity, and blood may be present as well. The chief cellular constituent is the lymphocyte.

Treatment.—The treatment of chyluria should be conducted

Digitized by Google

on the same lines as the treatment of inaccessible varix elsewhere; that is to say, by resting and elevating the affected part, and thereby diminishing as far as possible the hydrostatic pressure in the distended vessels. Many forms of medicinal treatment have been advocated. Because during treatment with some drug a chyluria has subsided, curative properties are apt to be attributed to the drug. The best results are got by sending the patient to bed, elevating the pelvis, restricting the amount of food and fluid—especially fatty food—gentle purgation, and absolute rest. It will be found that a day or two of treatment on these lines is often followed by temporary, perhaps prolonged, cessation of the chyluria. The drugs which have been particularly lauded in the treatment of this disease are gallic acid in large doses, benzoic acid in large doses, glycerin, the tincture of the perchloride of iron, decoction of mangrove bark, chromic acid, quinine, salicylate of soda, ichthyol, and *Nigella sativa*. Manson does not believe that these substances have any influence whatever in stopping the lymphorrhagia. Neither does he believe that thymol, recommended by Lawrie, or methylene-blue, recommended by American writers, has any effect either on the filaria or on the disease it gives rise to; since their first recommendation both drugs have been tried, but in other hands have failed.

Filarial orchitis, endemic funiculitis, and hydrocele.—A special form of inflammation of the testes was originally described by French writers as "malarial orchitis," and here and there in Indian medical literature allusion is made to the same or a similar subject. The Editor has many times seen filarial orchitis, but it is doubtful whether orchitis of purely and unquestionably malarial origin occurs. The fever attending filarial orchitis—which is usually associated with lymphangitis of the spermatic cord—has been described as a separate disease (endemic funiculitis, Castellani and Chalmers), but it is undoubtedly of filarial origin. It may be attended with inflammation of the scrotum, and, like ordinary elephantoid fever, resemble very closely a malarial attack, and may be mistaken for this. In cases of recurring orchitis of filarial origin with pyrexia, adenitis, and rigors, the Editor demonstrated large numbers of microfilariæ in the tunica vaginalis, at the commencement of each attack. The aspirated fluid is cloudy, contains a number of polymorph cells, occasionally erythrocytes with sheathed microfilariæ as well as others which have cast their sheaths. In these cases the epididymis is enlarged and nodular. In section the Editor has demonstrated dead and calcified filariæ blocking the vasa efferentia and causing extensive fibrotic changes.

Digitized by Google

It is possible that sterility is a direct result of the invasion of the genital organs by filariæ.

Recurrent attacks of filarial orchitis lead sooner or later to hydrocele. This condition is extremely common in association with elephantiasis of the scrotum. Among the Polynesians filarial hydroceles are common, especially in certain districts. The walls of the sac are thickened and contain calcified remains of adult filariæ; the fluid is clear and straw-coloured, and usually contains microfilariæ or their remains, though, from the rapidity with which these embryos die in hydrocele fluid, it does not seem to be a medium particularly favourable for their prolonged life.

Filarial synovitis. — Maitland mentions acute synovitis of the knee-joint as one of the filarial diseases, and gives the particulars of five cases. He considers the concurrence of synovitis with filarial invasion too common to be accidental. The Editor confirmed this, and has found that fibrotic ankylosis often results. In cases where the hip-joint is affected, removal of the inflamed iliac glands draining the area appears to relieve the condition.

In severe cases the synovitis may even proceed to pus-formation and a fatal result ensue.

Fugitive lymphatic swellings.—Among the rarer manifestations of *Filaria bancrofti* may be mentioned fugitive swellings resembling Calabar swellings, situated in the subcutaneous tissues in almost any part of the body. The Editor has seen them on the scalp, upper arm, and thigh, and occasionally in the muscular covering of the abdominal wall. Thrombosis of the larger veins and intramuscular hæmorrhages of considerable size have been noted.

ELEPHANTIASIS

Elephantiasis is by far the most frequent manifestation of filarial invasion, and is exceedingly common in some of the endemic districts. Thus, in certain districts in Cochin about 5 per cent. of the population, in Samoa about every second individual, in Huahine seven-tenths of the adult male population are affected. In the Ellice Islands, McNaughton reports that out of a total population of 3,434, 90 are affected by elephantiasis. In many other tropical and subtropical countries, if not so common as in those just mentioned, elephantiasis is, nevertheless, common enough.

Parts affected.—In 95 per cent. of the cases the lower extremities —either one or both—alone, or in combination with the scrotum or arms, are the seat of the disease. The foot and ankle only,

Digitized by Google

or the foot and leg, or the foot, leg, and thigh, may each, or all, be involved. The scrotum is also a common situation for elephantiasis. The arms are more rarely attacked; still more rarely the mammæ, vulva, and circumscribed portions of the integuments of the limbs, trunk, face (Fig. 161), neck, or scalp (Fig. 162). In Fiji, however, elephantiasis of the arm is comparatively common:

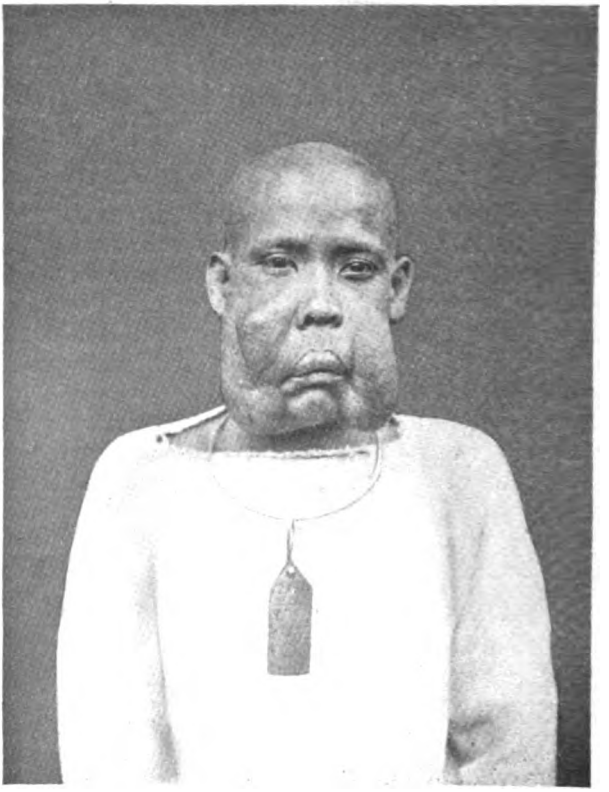


Fig. 161.—Elephantiasis of the cheeks. (*By permission of the London School of Tropical Medicine.*)

out of 47 cases the arms alone were affected in 10, both arms and legs in 6 cases.

The recurring erysipelatoid attacks.—The disease in any of these situations commences with a rapidly evolved lymphangitis, dermatitis, and cellulitis accompanied by elephantoid fever. On the subsidence of the acute symptoms the skin and subcutaneous

Digitized by Google

fascia of the affected part do not quite resume their original proportions; the inflammatory effusion not being completely absorbed, some permanent thickening remains. Recurrences of this inflammation once or twice a month, or perhaps once in six months, or every twelve months, or even at longer intervals, add a little each time to the bulk of the limb or scrotum. Thus, gradually, an enormous swelling may be built up. Occasionally, though very rarely, enlargement may progress after one, two, or more initial inflammatory attacks, and without further recurrence of these.

Clinical characters of the swelling.—The affected part is greatly increased in bulk. The surface of the skin, in confirmed elephantiasis especially, is rough and coarse; the mouths of the follicles are sometimes unusually distinct; the papillæ and glands are either hypertrophied or atrophied; the hair is coarse and sparse; the nails are rough, thick, and deformed. Around joints the thickened integuments are thrown into folds, the comparatively smooth-sided and deep interlying sulci permitting limited movement. There is no distinct line of demarcation between healthy and diseased skin. The implicated integuments are hard, dense, pit but slightly if at all on pressure, and cannot be pinched up or freely glided over the deeper parts.

Its macroscopic anatomy.—On cutting into the swelling, the derma is found to be dense, fibrous, and enormously hypertrophied. The subjacent connective tissue is increased in bulk, having, especially in the case of the scrotum, a yellowish, blubbery appearance from lymphous infiltration. A large quantity of fluid wells out on division of such tissues. The muscles, nerves, and bones are not necessarily diseased, although in rare instances they may be degenerated and slightly or considerably atrophied from pressure. The blood-vessels are large; the lymphatics dilated; the associated lymphatic glands, both of the same side and, very often, of the opposite side, enlarged and dense.

True elephantiasis permanent.—Though in recent cases the bulk of the limbs may be much reduced temporarily by treatment, the disease is never permanently recovered from. Simple lymphatic œdema in areas which have never become inflamed subsides readily enough on pressure or elevation.

Elephantiasis of the legs (Fig. 163).—Elephantiasis of the lower extremities is usually, though by no means always, confined to below the knee. The swelling may attain enormous dimensions and involve the entire extremity, the leg or legs attaining a circumference, in aggravated cases, of several feet.

Digitized by Google

Treatment.—In the treatment of elephantiasis of the leg the patient should be encouraged to persevere with elastic bandaging, massage, and elevation of the limb. Ligature of the femoral artery has been practised; it is probably useless, and is certainly not a justifiable method of treatment. Sometimes, in extreme cases, good results are got from excision of redundant masses of skin, a longitudinal strip of three or four inches in breadth by a foot or more in length being dissected off. Charles advocated complete resection of the whole of the elephantoid tissue, except the sole of the foot, followed by extensive skin-grafting. Electrolysis and mercury have also been used: one questions their value. During the acute attacks, tension may be relieved by aseptic punctures with a sharp lancet. At all times the limb must be carefully guarded from injury, and shoes and trousers worn. Slight injuries provoke the inflammatory recurrences. Wading in water, prolonged standing, violent exercise, and exposure to a hot sun are injurious and should be avoided.

Fig. 162.—Elephantiasis of scalp. ("*Journ. of Trop. Med.*")

Handley's operation.—Handley has brought forward an operation, lymphangioplasty, the underlying principle of which is the drainage of an area of lymph stasis into an adjacent patent lymphatic area by means of strands of silk passing from one to the other. He describes the operation thus: "Eight stout silk threads were led upwards from the foot to a point in the iliac fossa just above Poupart's ligament. These were spaced round the limb at intervals. Above they united to form a leash. The iliacus muscle was exposed by a short incision like that for ligature of the external iliac artery. Half the threads were passed through a portion of the iliacus muscle, and were knotted in pairs to the other four threads, thus fixing them securely to the tissues of the iliac fossa. The multiple small incisions through which the threads were introduced were closed by horsehair sutures, leaving the silk completely buried in the subcutaneous tissues." He claims a comparative success in one marked case of elephantiasis of the leg. Judging from the narrative of this case the operation is attended with considerable risk from sepsis. Others who have practised it do not report favourably on the results.

Digitized by Google

Lanz's operation aims at deep lymphatic drainage. A longitudinal incision is made through the fascia lata down to the femur, the periosteum of which is stripped and the bone trephined in several places; strips of fascia are then inserted into the openings thus made. Surgeons who have followed this method report excellent results; many have omitted trephining the bone and have contented themselves with incising the fascia lata.

Kondoleon's operation consists also of free incision of the fascia

Fig. 163.— Elephantiasis of legs; scrotum and right arm also affected. (*Photo: Dr. Turner, Samoa.*)

lata and removal of large sections of the aponeurosis; the removal of this tissue assists in the anastomosis of lymph channels and veins. This operation has been favourably reported on by Matas.

Elephantiasis of the scrotum (Fig. 164). *Weight of tumours.*—Elephantiasis of the scrotum, or "scrotal tumour" as it is sometimes called, may attain an enormous size: 10, 15, 20 lb. are common weights for these tumours, and 40 or 50 lb. is by no means uncommon. The largest recorded weighed 224 lb.

Anatomical characters.—There are certain points in the anatomy of scrotal tumour which the operating surgeon must bear in mind. These tumours con-

Digitized by Google

sist of two portions (Fig. 165): first, a dense rind of hypertrophied skin (A *e*) thickest towards the lower part and gradually thinning out as it merges above into the sound skin of the pubes, perineum, and thighs; second, enclosed in this rind, a mass of lax, blubbery, dropsical, easily-torn-through, areolar tissue in which testes, cords, and penis are embedded. The shape of the tumour is more or less pyriform. The upper part, or neck, on transverse section (B) is triangular, the base (B *k*) of the triangle being in front, the apex (B *j*)—usually somewhat bifid from dragging on the gluteal folds—towards the anus, the sides (B *h*) towards the thighs. In the latter situation the skin, though

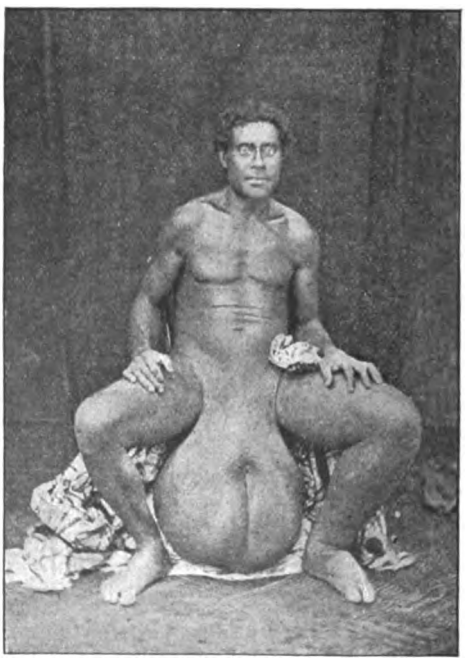


Fig. 164.—Elephantiasis of scrotum; left leg slightly affected. (*Photo: Dr. Turner, Samoa.*)

usually more or less diseased, is, from pressure, softer and thinner than elsewhere, tempting the surgeon to utilize it for the formation of flaps—not always a wise proceeding. The penis (A *a*, B *f*) always lies in the upper and fore part of the neck of the mass; it is firmly attached to the pubes by the suspensory ligament. The sheath of the penis is sometimes specially hypertrophied, standing out as a sort of twisted ram's-horn-like projection on the anterior surface of the tumour; this, however, is unusual. Generally the sheath of the penis is incorporated in the scrotal mass, the prepuce being dragged on and inverted so as to form a long channel leading to the glans penis and opening (A *l*) half-way down, or even lower, on the face of the tumour. The testes (A *c*), buried in the central blubbery tissue, usually lie

Digitized by Google

towards the back of the tumour, one on each side—in large tumours generally nearer the lower than the upper part. They are more or less firmly attached to the under part of the scrotum by the hypertrophied remains of the gubernaculum testis (A *d*)—a feature to be specially borne in mind by the surgeon. As a rule both testes carry large hydroceles with thickened tunicæ vaginales. The spermatic cords also (A *b*, B *g*) are thickened and greatly elongated.

The arteries which supply these enormous growths are of considerable size; the veins, too, are very large, and, as they permit regurgitation of blood from the trunk, are apt to bleed freely.

Their importance.—Beyond the inconvenience caused by their weight, the presence of the cumbersome mass between the legs, the suffering attendant on recurring attacks of inflammation and elephantoid fever, the sexual disability, and the unsightliness, these tumours are not of great importance; they do not, as a rule, directly endanger life. They may grow rapidly or slowly; they may attain a large size in two or three years, or they may be in existence for years and at the end of this time amount to little more than a slight thickening of the scrotum. Occasionally, in large tumours, portions of the mass become gangrenous, or abscess may form, and in these ways life may be endangered.

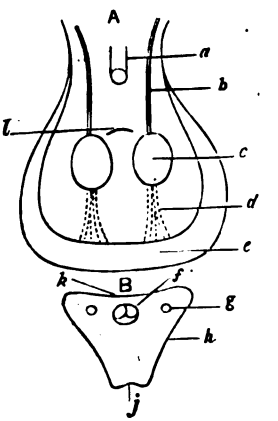


Fig. 165. — Diagram of anatomy of elephantiasis of scrotum. (For references, *see* text.)

Treatment.—Scrotal tumour, as soon as it becomes unsightly or inconvenient, should be removed. Often, after thorough removal of all the diseased integuments, elephantoid fever, which before may have been frequent, ceases to recur.

Treatment preliminary to operation.—If the tumour is of considerable size the patient should keep his bed for a day or two before operation, the mass being suspended so as to drain it of fluid and blood. It is thus rendered lax, and the operator is enabled to ascertain by palpation the position of the testes and, if such chance to be present, of hernia—a not very unusual complication. The possibility of undescended testes should not be overlooked.

Operation.—Before making provision for the prevention of hæmorrhage the operator should mark out by shallow cuts the line at which he proposes to separate the tumour, care being taken that these guiding incisions run through and include only absolutely sound skin. If the latter precaution be neglected, disease is very liable to recur in the scar or flaps. First, the tumour is turned up and a shallow transverse cut is drawn in sound skin

Digitized by Google

across the perineum in front of the anus. The tumour being allowed to fall down, a similar shallow cut is made across the pubes. The corresponding extremities of these two cuts are then united either by a straight cut, or, if there be a little sound skin on the thigh aspects of the tumour, by semilunar incisions.

Assistants then firmly draw down the scrotum as far as possible, and the surgeon, if he deem it desirable, applies elastic webbing over the mass so as to expel the blood it contains. Next, a stout rubber cord is wound, figure-of-eight fashion, round the neck of the tumour, well above the guiding incisions, and over the pelvis, and firmly secured (MacLeod) (Fig. 166). Or the rubber cord

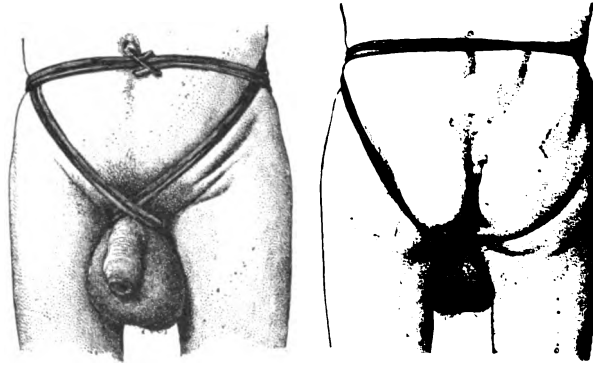


Fig. 166.—Rubber cord in position. (*MacLeod.*)

is wound round the neck of the tumour only, being kept in place by four strips of bandage passing under this cord, one on each side of the scrotum before and behind, and firmly tied over another strip of bandage encircling the waist.

The testes and spermatic cords are first dissected out through long perpendicular incisions made in front, the remains of the gubernacula testium being hooked up with the finger and snipped through with scissors. The channel of the prepuce is next slit up, the incision being carried up to the pubic limiting mark. The penis can then be shelled out, the prepuce being first cut through around the corona glandis. If lateral flaps can be formed of sound skin, they are then dissected up. The perineal and pubic incisions are now deepened and, assistants holding the testes and penis well out of the way, the neck of the tumour is cut through close to the perineum and pubes. Gaping vessels are all carefully

Digitized by Google

ligatured, redundant tunica vaginalis—if hydroceles be present —being excised. The rubber cord is then removed.

When hæmorrhage has been controlled, the posterior halves of the flaps are brought together by sutures, the anterior halves being united, over the testes, to the pubic cut. The penis will therefore emerge from the point where the horizontal line meets

Fig. 167.—Elephantiasis of right arm and hand in a Fijian. (*Orig.*)

the perpendicular line of what is now a T- or Y-shaped wound. If no flaps have been made, the testes may be fixed by stitching any tag of tissue connected with them to the perineum, and the dimensions of the wound reduced as much as possible by stitching up the corners at the pubes and perineum.

In dressing it is of importance that the raw surfaces be covered by some aseptic *non-fibrous* protective—such as oiled silk—before the antiseptic dressing is applied. A fibrous dressing next

Digitized by Google

the raw surfaces is troublesome, as it sticks to the wound and is painful and difficult to remove. The dressing should be massive, well padded, and kept in place by an eight-tailed bandage secured in front and behind to a strap round the waist, a hole being cut in front for the penis to emerge. The large wound generally does well. Skin-grafting should be practised freely and early, especially round the root of the penis.

Mortality from operation.—The mortality from these formidable-looking operations, if they are carefully done, is small, and need not exceed 5 per cent. The results are very satisfactory as a rule, the functions of the organs being retained or restored.

Elephantiasis of the arms.—This is comparatively rare. Allowing for the differences between the upper and lower extremi-

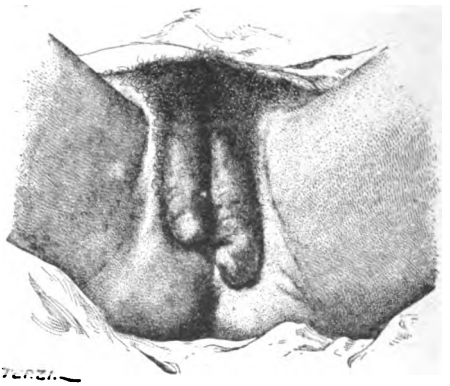


Fig. 168.—Elephantiasis of labia majora. (*After Nuñez.*)

ties as regards gravitation of fluids, the symptoms and pathology of elephantiasis of the arms are the same as those of elephantiasis of the legs. Beyond the judicious employment of massage and elastic bandaging, little can be done in the way of treatment. (Fig. 167.)

Elephantiasis of the vulva and mammæ.—Elephantiasis of the vulva (Figs. 168, 169) and mammæ (Fig. 170) is still rarer. Where growth has become inconveniently large the diseased tissues should be removed. Instances are on record in which the integuments of the mammæ have become so thickened, heavy, and elongated that the organ has descended to the pubes and even to the knee. One such tumour weighed 21 lb. after removal. Tumours of the labia or of the clitoris, similarly, may attain a great size—8 or 10 lb., or even more.

Digitized by Google

Elephantiasis of limited skin areas.—Corney states that pedunculated elephantoid tumours, springing from the groin or from the anterior surface of the thigh, are not uncommon in

Fig. 169.—Elephantiasis of vulva. (*Photo: Dr. Walter H. B. Macdonald.*)

Fiji. One such tumour which he removed weighed 20 lb. Daniels has seen, both in Fiji and in Demerara, several cases of this description (Fig. 171). Silcock describes a pedunculated tumour of this

Digitized by Google

nature which he removed from the neck of an East Indian, and which weighed, after removal, 30 lb. Manson has seen limited areas of elephantoid thickening of the skin, particularly on the thighs. These conditions are easily dealt with by simple operations.

Fig. 170.—Elephantiasis of mammæ; left leg and foot also affected. (*Photo: Dr. Davies, Samoa.*)

Chylous dropsy of the tunica vaginalis, and of the peritoneum; chylous diarrhœa. — Chylous dropsy of the tunica vaginalis is not an unusual occurrence in the tropics. A fluctuating swelling of the tunica vaginalis, which does not transmit

Digitized by Google

light, and which is associated possibly with lymph scrotum, with varicose groin-glands, with chyluria, or with microfilariæ in the blood, would suggest a diagnosis of this condition. These collections of chylous fluid in the tunica vaginalis generally contain enormous numbers of microfilariæ. Large numbers of cretified adult filariæ have been found in the thickened tunica vaginalis and in the epididymis in this condition.

These chyloceles may be treated as ordinary hydroceles, either by aseptic incision or by injection.

Fig. 171.—Pedunculated groin elephantiasis.
(Photo: Dr. Daniels.)

Filarial orchitis with effusion into the tunica vaginalis, according to Maitland, is best treated by incision of the tunica vaginalis, turning out any clot that may be found in the sac, and stuffing the latter with iodoform gauze. This procedure, he says, gives immediate relief.

Chylous dropsy of the peritoneum and chylous diarrhœa of filarial origin are very rare.

Medicinal treatment of filariasis.—It must be confessed that there is not, at present, any drug known to be specific for *F. bancrofti*. Rogers reported that a considerable reduction in the

Digitized by Google

number of circulating microfilariæ took place as a result of intensive treatment with large doses (30 gr.) of antimony tartrate spread over a period of six weeks. In other cases the drug had no such effect.

In view of the fluctuation of these embryos in the blood of untreated filariated subjects, it is unjustifiable to regard any diminution in their numbers as necessarily due to the action of any particular drug. There is no evidence to show that any drug has caused the death of the adult filaria.

Prophylaxis of filarial disease.—The prevention of filarial disease resolves itself into anti-mosquito measures and protection from mosquito-bite. With this in view, unprotected wells, tanks, or stagnant pools must not be permitted in the neighbourhood of dwelling-houses. All vessels used for storing water should be emptied at least once a week. The mosquito-net is indispensable in filarial as well as in malarial countries.

The subjects of filariasis should be regarded as dangers to themselves and to the community and be compelled to sleep under mosquito-nets.

Digitized by Google

CHAPTER XLII

PARASITES OF THE LYMPHATIC SYSTEM AND CONNECTIVE TISSUES

FILARIASIS (*concluded*)

2. Loa loa (Guyot, 1778)

History.—*Loa loa* has been known for more than three hundred years. Although undoubtedly of African origin, the earlier-described cases were in negroes in the West Indies who must have acquired their parasites in West Africa prior to their deportation as slaves to America. For long the worm was regarded as an immature dracunculus. Since the characters of the parasite have been more carefully studied this view can no longer be held, and *L. loa* is now thoroughly established as a distinct species.

In 1891 Manson found in the blood of two negroes—one from the Lower Congo, the other from Old Calabar—certain microfilariæ morphologically closely resembling that of *F. bancrofti*, but differing from the latter inasmuch as they came into the peripheral circulation during the day and disappeared from it during the night. As in one of these negroes *L. loa* had formerly been seen in his eye, Manson suggested that the new microfilaria, which he named *F. diurna*, was the embryonic form of *L. loa*. This view was supported by the fact that in fragments of a loa received from Leuckart the contained embryos appeared to be identical in every respect with *F. diurna*. Nevertheless, Manson failed in several cases of *L. loa* infection to find *mf. diurna* in the blood.

Later, an association was discovered between *L. loa* and the disease known as Calabar swellings, and also between Calabar swellings and *mf. diurna*. As a considerable number of cases of *L. loa* concurring with *mf. diurna* have been recorded, and by many observers, and as *mf. diurna* and the microfilariæ in the uterus of *L. loa* are morphologically indistinguishable, there can be little doubt that *L. loa* and *mf. diurna* are respectively the mature and embryonic forms of the same species.

Geographical distribution.—We have fairly definite knowledge of the extent of the geographical range of *L. loa*. It appears to be widely distributed throughout tropical West Africa from Sierra Leone to Benguella. In some parts—as in Old Calabar,

Digitized by Google

Cameroons, and the Ogowé River a very large proportion of the inhabitants are affected. How far it penetrates into the interior of the continent is as yet unknown. Manson has seen several cases in Europeans from the Upper Congo within a few miles of Stanley Falls. Brumpt records its presence in Kassai, approximately 600 miles from the coast, on one of the chief tributaries of the Congo. The larval form (*mf. loa*) has been found twice by Cook in Uganda, although such isolated findings cannot be taken as landmarks, seeing that *L. loa* is a long-lived parasite and its hosts may have contracted the infection years previously, and at a distance from the place at which it was recognized. At the time of the slave trade numerous cases were reported from the West Indies and South America, but always in negroes from Africa, and their occurrence ceased with the abolition of slavery. The suggestion that about 1795 there existed an endemic centre for this parasite in San Domingo is based on very doubtful evidence. Nowadays, cases are occasionally seen in Europe and America, in both negroes and whites, but only in persons who have frequented those parts of Africa inhabited by the parasite. Possibly, on account of the opening of new trade routes and of the more frequent intercourse between the natives, *L. loa* may greatly extend its range in Africa.

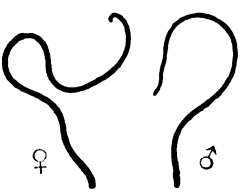


Fig. 172.—Loa loa. Nat. size.

The parasite (Fig. 172).—A minute description of the adult *L. loa* is given in Appendix II., p. 839. Here it suffices to say that they are 30 mm. or more in length, the female being, as a rule, considerably longer than her partner. The cuticle is embossed with numerous characteristic protuberances.

Structure of the embryonic form.—*Microfilaria loa* (= *diurna*) is very similar in size (298 μ by 7·5 μ) and structure to *microfilaria bancrofti*. Like the latter, it is enclosed within a "sheath," its tail is pointed, and it has the same V and tail spots.

Their respective periodicities are very characteristic—more so, apparently, in the case of *mf. loa* than in that of *mf. bancrofti*; for, whereas by inverting the sleeping habits of a subject of *F. bancrofti* infestation it is easy to invert or disturb the periodicity of the microfilariæ, this has not been done in the case of *mf. loa*. Unfortunately, only one experiment can be adduced in support of this remarkable circumstance; but this experiment was very thoroughly and carefully conducted, and extended over a considerable period. During all the time the patient (who had had several loas excised at different times and who was still showing signs of their presence) slept during the day and kept awake during the night; nevertheless, the microfilariæ continued to appear in vast numbers in the peripheral blood during the day, but were only very rarely found in it during the night. (Chart 31.)

Digitized by Google

Attitudes (1) of mf. bancrofti, (2) of mf. loa; heads (3) of mf. bancrofti, (4) of mf. loa; tails (5) of mf. bancrofti, (6) of mf. loa.

DISTINGUISHING FEATURES BETWEEN MF. BANCROFTI AND MF. LOA, IN STAINED SPECIMENS.

PLATE XXV.

Digitized by Google

Digitized by Google

Although in the fresh liquid blood it is practically impossible to distinguish, with the microscope alone, the living *mf. loa* from the living *mf. bancrofti*, in dried and stained films certain more or less pronounced differences can be made out. (1) In such preparations *mf. bancrofti* is usually disposed in sweeping and graceful curves, such as a skilled penman might make (Plate XXV., Fig. 1); *mf. loa*, on the other hand, assumes a stiff, ungraceful, almost angular attitude, like the flourishes made by a schoolboy (Plate XXV., Fig. 2). (2) The tail end of *mf. loa* is often disposed in a series of sharp flexures, giving it in some instances a corkscrew-like appearance, the extreme tip being always sharply flexed (Plate XXV., Fig. 6). (3) The nuclei of the central column of cells of *mf. loa* are larger and stain less deeply than those of *mf. bancrofti*, and, as a rule, the cephalic end of the column is more abruptly terminated in the former. Although in most slides one or two specimens may be hard to diagnose, on the average of a series of preparations the foregoing distinctions are recognizable. Fülleborn by special staining methods points out various minor differences (Fig. 139),

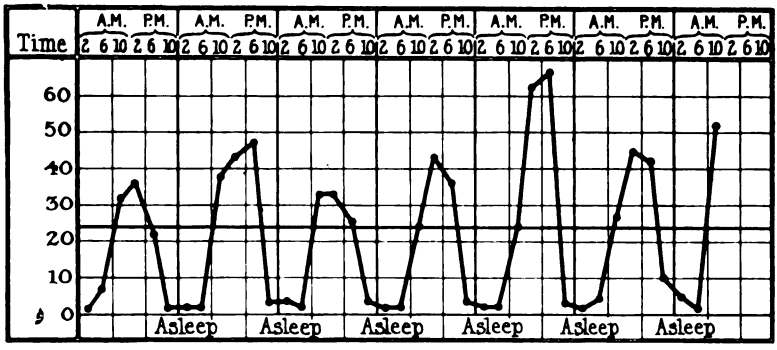


Chart 31.—Diurnal periodicity of microfilaria diurna (mf. loa). (*Orig.*)

The numbers in the first column are those of the microfilariæ per 16 c.mm. of blood.

amongst which the large genital cell is a marked feature. He proposes the measurement of various fixed points (Fig. 326, p. 837) as a standard of differentiation of the various microfilariæ.

Life-history of L. loa.—In early editions of this book Manson called attention to the so-called mangrove fly, *Chrysops dimidiata* (Fig. 173) as a possible intermediary on account of its diurnal and blood-sucking habits and local distribution. This conjecture Leiper has ascertained to have been well founded. During a visit to West Africa, with the object of ascertaining the intermediary host of *L. loa*, he examined many blood-sucking insects, including mosquitoes and a variety of others. He found that in the salivary glands of *Chrysops dimidiata* and in *C. silacea*, and, as later researches have shown, probably of *C. longicornis* as well, rapid and uniform developmental changes of *mf. loa* were effected, similar to those of *mf. bancrofti* in the mosquito. Later observations by Kleine, working in the Cameroons, tend to confirm those of Leiper. As to the exact manner in which *L. loa* is acquired we must await further information.

It would appear that, after it has entered the human body, development

Digitized by Google

is very slow, and that probably full maturity is not attained until after several years. In many cases the parasite did not show itself until 3, 4, and 4½ years after the patient had left the endemic area. In one case the parasite was extracted from the eye 13 years after the patient had left Africa; in another the worm or worms appeared at irregular intervals during 15 years. Manifestly it is long-lived. An interesting and suggestive evidence of slow development is that, while the immature active worm is often seen in children, the larval form in the blood is found as a rule only in adults. Annett, Dutton and Elliot, in 390 native children of all ages up to about 18 years, examined in a district where *L. loa* was exceedingly common in adults, found *mf. loa* once only, in a boy aged 11. Meinhof reports a case in which the period elapsing between infection with *F. loa* and the appearance of embryos in the blood was at least 7 years.

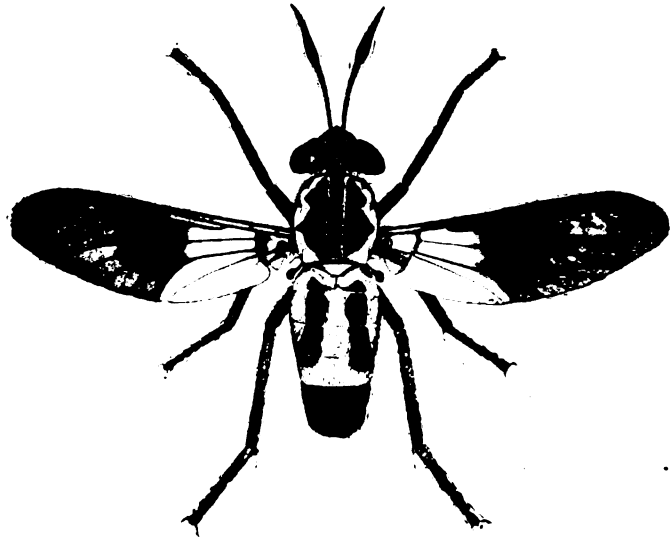


Fig. 173.—Chrysops dimidiata (v. d. Wulp), ♀. × 5 diameters.

Slow development and a different habitat at different stages are not peculiar to *L. loa* alone. *F. equina* of the horse and ass and *F. labiato-papillosa* of deer and cattle wander about the subdermal connective tissues and frequently occur in the eyes during their semi-adult stage, but repair to the peritoneal cavity when fully mature. The larvæ of both are found in the blood of the respective hosts, and Noé has shown recently that *F. labiato-papillosa* is fostered and transmitted, like *F. bancrofti* and *F. immitis*, by an insect intermediary (*Stomoxys calcitrans*), amongst the cephalic muscles of which it undergoes development.

This slow development of *L. loa* would seem to account for the very frequent failure to find the microfilariæ in the blood in cases from which mature parasites have been extracted, a circumstance which has been brought forward as an argument against the theory that *mf. diurna* is really the offspring of *L. loa*. Years ago Manson was consulted by a lady who for seven years had

Digitized by Google

been troubled with *L. loa* and Calabar swellings, and had had three loas removed at different times from the neighbourhood of the eye. On examining her day blood he found innumerable specimens of *mf. diurna*. That these microfilariæ were *diurna* was fully established by a series of carefully conducted observations carried on day and night for upwards of a week. Later, Manson had an opportunity of examining the worm removed from one of her eyes seven years previously. It was a mature female crowded with embryos in all stages of development, including free larval forms such as were found in the blood. It transpired that with a negative result, many years before, Manson had examined the day blood of this patient soon after this extraction had been made. From this it is evident that the mature *L. loa* may be present in the tissues, and yet that embryos may be absent from the blood. An explanation of what is apparently an anomaly cannot at present be suggested; but the fact is definitely ascertained, and explains how it is that in many of the recorded cases of loa infestation the embryos have been absent from the general circulation. It may be that it is not until the gravid female arrives at some organ or tissue that she deposits her young in such a position that they can get access to the circulation, and that the wanderings for which these worms are so remarkable are an effort to attain this situation. It would be well that those who have the opportunity should look for the parasite at autopsies, especially in the serous cavities. Penel stated that he had found *mf. loa* in the saliva and urine of a patient who presented this embryonic filaria in the peripheral circulation.

As yet it is impossible to estimate accurately the number of adult loas present in any given infection, although in advanced cases some idea of this might be got from the number of microfilariæ in the peripheral blood. As a rule it is safe to conclude that the particular loa that may show itself about the eye or elsewhere is only one of many. Thus, in 1903, Brumpt, at the post-mortem of a negro whose blood contained microfilariæ (for which, under the impression that it was a new species, he suggested the name of *F. bourgi*), found in the tissues of the heart five adult worms. Four of these were cretified, but the fifth was alive and contained embryos similar to those in the blood. This worm he subsequently identified as a *L. loa*. In the following year Wurtz found *mf. diurna* in the blood of a Congolese negro suffering from sleeping sickness. On the death of the patient he made a most careful post-mortem examination, and found two adult loas in the subcutaneous connective tissue of the arm. On the dissection being continued by Penel, over thirty additional specimens, male and female, were discovered under the skin of the limbs. There are not a few instances on record in which two or more loas have been extracted from the same patient. We may, therefore, be practically certain that in nearly every instance of this kind of filariasis the infection is multiple.

There is evidence that after the death of *L. loa* calcification takes place, as in *F. bancrofti*.

Pathogenesis.—As already stated, *L. loa* during the period of its growth and development in man makes frequent excursions through the subdermal connective tissues. It has been noticed very frequently beneath the skin of the fingers, and it has been excised from under the skin of the back, from above the sternum, from the left breast, the lingual frænum, the loose skin of the penis,

Digitized by Google

the eyelids, the conjunctiva, the anterior chamber of the eye. Ziemann says that it may wander about the scalp. The parts most frequently mentioned are the eyes, and, although the worm may have attracted more attention when in this situation, it seems as though it has a decided predilection for the eye and its neighbourhood. A patient of Manson's once stated that the average rate at which a loa travelled was about an inch in two minutes. Both he and others have stated that warmth, such as in sitting before a fire, seemed to attract them to the surface of the body. As a rule, the migrations of the parasite give rise to no serious inconvenience, but they may cause prickings, itching, creeping sensations, and, occasionally, transient œdematous swellings ("Calabar swellings") in different parts of the body. When the parasite appears under the conjunctiva it may cause a considerable amount of irritation and congestion; there may be actual pain even, associated with swelling and inability to use the eye and, perhaps, tumefaction of the eyelids. Should a loa wander into the vicinity of such a situation as the rima glottidis or the urethra the consequences might be serious.

CALABAR SWELLINGS

Under this name Thompstone described certain fugitive swellings which are of frequent occurrence in parts of tropical West Africa—Southern Nigeria to Benguella and inland to the Upper Congo. They are found in natives and Europeans alike. Manson has seen many cases in Englishmen, especially in officials from the neighbourhood of Old Calabar. Thompstone says: "The swellings are about the size of half a goose egg, painless, though somewhat hot both objectively and subjectively, not pitting on pressure, and usually disappear in about three days. They come suddenly and disappear gradually, and occur in any part of the body." This observer never saw more than one swelling at a time. They recur at irregular intervals and, it may be, during many years after the patient has returned to Europe. In some instances the swellings seem to be induced by the rubbing provoked by the irritation accompanying the presence of a *L. loa* just under the skin, in other instances they develop spontaneously. When occurring in the hand, or about the forearm, they may give rise to a sensation of powerlessness and soreness as if the part had received a blow. They never suppurate.

Although in a large proportion of cases *L. loa* larvæ cannot be found, in others either the parent worm has shown itself in the eye or its microfilariæ have been detected in the blood. The

Digitized by Google

latter circumstance, together with the geographical feature of the endemicity of these swellings and their clinical characters, makes it practically certain that they are somehow produced by *L. loa*. On the supposition that the swelling might be caused by the emission of her larvæ by a parent loa into the connective tissue, Manson once endeavoured, by aspirating the centre of the swelling with a hypodermic syringe, to substantiate this speculation; the result was negative, but a second attempt on another patient yielded great numbers of microfilariæ in the lymph abstracted. Notwithstanding this success, it cannot be affirmed that the mechanism of the production of Calabar swellings has been solved.

A *general œdema* of one limb may ensue; lately the Editor has seen an officer who contracted loa in the Cameroons during the recent war, and who suffered from a fugitive elephantoid condition of the left leg, together with permanent and painful swellings of both forearms. Curious cyst-like and tender lymphatic swellings were observed also in this same case over the flexor tendons of the forearm and the peronei of both legs; in the latter situation they increased in size in the erect posture.

3. Human Onchocerciasis

Onchocerca volvulus (Railliet and Henry, 1910)

History.—*Onchocerca volvulus* was discovered by a German medical missionary, in two tumours the size of a pigeon's egg, which he had removed, one from the scalp, the other from the chest of Gold Coast negroes. The tumours were forwarded to Leuckart, who described and named the parasite *Filaria volvulus* in 1893. In 1899 Labadie-Lagrave and Deguy found an immature female filaria, which Blanchard identified as *O. volvulus*, in a small tumour removed from the arm of a soldier who contracted the infestation six years previously in Dahomey; they were able to show that the parasite occupied a lymphatic vessel. In 1901 Prout described two cases from Sierra Leone. Brumpt, during his travels through Central Africa, had the opportunity of examining numerous cases. Recently Fülleborn and Parsons have added considerably to our knowledge of this parasite. Other species, such as *O. gibsoni*, are parasitic in cattle and give rise to small nodes in beef. It has been suggested by Cleland that this latter species is transmitted by *Stomoxys*.

Geographical distribution.—The earlier cases were reported from the West Coast of Africa—Sierra Leone, Gold Coast, Dahomey. Brumpt met with his cases along the Welle between Dongon and

Digitized by Google

M'Binia. He believes that in that region *O. volvulus* affects about 5 per cent. of the riverine population. He saw cases on the Himbri, and he refers to others on the Kibali and on several of the tributaries of the Welle. Cook met with cases in Uganda, Fülleborn in the Cameroons, Parsons in Northern Nigeria. Clapier has reported cases from French Guinea and also from the French Sudan (Dakar). In 1915 Robles recognized the occurrence of *O. volvulus* in Guatemala. Caldéron (1920) defined the endemic zones as being in the departments of Sacatapéquez, Escuinthla, and Sololá, at an altitude of 2,800–3,600 feet. It is suggested that the parasite was originally imported by negro slaves from Jamaica.

The parasite.—The worms are white in colour and filiform, tapering at both ends. They vary considerably in length, the female, as in the case of all the filariæ, being much the longer (60–70 mm.). The body is transversely striated. At least four males and two females are present in every tumour. On account of the large size of the spicule in the male it has been suggested by Caldéron that *O. volvulus*, as it occurs in South America, constitutes a separate species. The unsheathed embryos measure about 300 μ in length.

Life-history. — Nothing is known of the life-history of this filaria. Recently, embryos, presumably those of *O. volvulus*, have been found in the peripheral circulation by Fülleborn, Simon, Ouzilleau, and Rodenwaldt. Brumpt, from the examination of numerous sections of filarial tumours, is confident that the microfilariæ leave the cysts. He has seen them round the periphery of the tumours, and believes they may reach the lymphatics and thence the general circulation. He even suggests that the infection is transmitted by some blood-sucking insect, and, considering its riverine distribution, he points more especially to the glossinæ.

Pathogenesis.—*O. volvulus* is found in peculiar subcutaneous fibrous tumours, the size of a pea to that of a pigeon's egg. The same patient may present one or several of these tumours. The regions of the body most frequently affected are those in which the peripheral lymphatics converge. Thus the tumours are usually found in the axilla, in the popliteal space, about the elbow, in the suboccipital region, and in the intercostal spaces. In the South American form the occipito-frontal and temporal regions were noted to be most usually affected. They are never adherent to the surrounding structures and can be easily enucleated. They are formed of a dense mass of connective tissue, which enwraps the parasites and encloses small cyst-like spaces filled with a greyish viscous substance consisting almost entirely of microfilariæ. The position of the adult worms within these tumours is very remarkable. The greater length of the coiled-up bodies of the females is embedded in the connective stroma; consequently they cannot be extracted unless in fragments. The males lie in

Digitized by Google

the little cyst-like cavities in the tumours, and can be turned out entire. The posterior extremity of the male with its copulating organs, and the anterior extremity of the female with its vaginal opening, are free and contiguous in one of the spaces.

The formation of the tumours is elucidated by Labadie-Lagrave and Deguy's case. These authors found an immature female *O. volvulus* in a lymphatic vessel partly obstructed by an infiltration of fibrin and leucocytes. It appears, therefore, that the presence of the parasites within the lymphatics gives rise to an inflammatory process, and that the consequent fibrinous deposit envelops the parasites, obliterates the lumen of the vessel, and ultimately isolates the affected tract. According to the natives, the tumours may last indefinitely, and they seldom ulcerate or suppurate, though Schäfer has recently reported finding, in the Cameroons, portions of undoubted *O. volvulus* in deep muscular abscesses. Some old patients told Brumpt that their tumours had been present since childhood. (*See* Juxta-articular Nodules, p. 743.)

Ouzilleau concludes from some remarkable but unconfirmed observations that in the Mbomou region, Equatorial Africa, where *F. bancrofti* is absent or very rare, but elephantiasis, lymphocele, and lymph scrotum very common, *O. volvulus* is the cause of these diseases in that district. *Microfilaria volvulus*, he states, is invariably present in the enlarged inguino-crural glands.

Eye lesions.—In 1918 Pacheco Luna suggested that *O. volvulus*, in its migrations through the body, was responsible for a peculiar form of keratitis punctata commonly found in Guatemala. Caldéron has lately suggested that it produces lesions of the iris and cornea as well.

4. Dracontiasis

Dracunculus medinensis (Velsch, 1674)

Synonym.—Guinea-worm.

Geographical distribution.—This important parasite is found in certain parts of India—the Deccan, Scinde, etc.—in Persia, Turkestan, Arabia, tropical Africa—particularly on the West Coast, and in a very limited part of Brazil (Feira de Santa Anna). Formerly it was supposed to be endemic in Curaçao, Demerara, and Surinam; apparently it has now disappeared from these places. Dracunculus is not equally diffused throughout this extensive area; it tends to special prevalence in limited districts, in some of which it is excessively common. In parts of the Deccan, for example, at certain seasons of the year nearly half the popula-

Digitized by Google

tion is affected; and in places on the West Coast of Africa nearly every negro has one or more specimens about him. Although guinea-worm is sometimes seen in Europe, this is only in natives of, or in recent visitors from, the endemic areas. Though frequently introduced in this way, it has not become established either in Europe or in North America. We have no account of the parasite as endemic in any part of Asia east of Hindustan, in the Eastern Archipelago, in Australia, or in the Pacific islands.

Dracunculus medinensis has been reported from horses, oxen, dogs, wild cats, jackals, leopards, and other animals. Possibly some of the parasites in the lower animals described as guinea-worm may belong to quite a different species.

The parasite.—The male worm is much smaller than the female, and, according to Leiper, is only 22 mm. in length. The female measures about 32·5 cm. to 1 m. 20 cm. in length by 1·5 mm. in diameter. The tip of the tail is incurved to form a blunt hook. The embryos are somewhat flattened, with a tapering tail, and measure 0·5–0·75 mm. in length by 0·017 mm. in breadth. (For further details, *see* Appendix II., p. 844.)

The *embryos*, in swimming, move by a sort of side-to-side lashing of the tail, and tadpole-like motion of the body. The movements are intermittent, sudden short swims alternating with brief pauses. When progressing, the greater transverse axis of the body is perpendicular to the plane travelled over; but when, from time to time, the little worms pause, they gradually roll over on to their flat surfaces. As soon as they come to rest on the flat they suddenly recover themselves with a jerk, and turn quickly on to their edges and begin swimming about again. This series of movements is constantly repeated. The cuticle is very distinctly transversely striated. (Fig. 174.)

In clean water the embryo remains alive for six days; in muddy water or in moist earth it will live from two to three weeks. If slowly desiccated it does not die; it may be resuscitated by again placing it in a little water.

Life-cycle in intermediary host.—If, by way of experiment, we place some dracunculus larvæ along with *Cyclops quadricornis*, or allied species, in a watch-glass, we shall find that, after a few hours, the larvæ have transferred themselves to the interior of the body cavity of the cyclops, where they can be seen moving about, coiling and uncoiling themselves, with considerable activity (Fig. 175). As many as fifteen or twenty young guinea-worms may be counted in each of the little crustaceans, which, unless the infestation is excessive, seem in no way inconvenienced. After a time the embryos so transferred undergo a metamorphosis. They cast their skins two or three times, get rid of their long swimming tails, acquire a cylindrical shape, and ultimately, along with increased size, develop a tripartite arrangement of the extreme posterior end. This larva is 1 mm. in length.

Liston in some Indian villages found 38·6, and Chatton in Dahomey 100 per cent. of the cyclops in the village ponds and wells naturally infested. The last-named investigator has suggested that the same species of *Cyclops* does not necessarily form the most suitable intermediary host in the different countries in which the dracunculus is endemic. In Tunisia the appropriate species is *C. viridis*.

Digitized by Google

Mode of infestation.—The metamorphosis of *D. medinensis* in cyclops was discovered by Fedschenko in Turkestan. His observations Manson confirmed in England; but, owing to the colder climate of the latter country, the metamorphosis takes longer to complete—eight or nine weeks, instead of five weeks as in Turkestan. Fedschenko supposed that the cyclops containing the larvæ of the guinea-worm, on being swallowed by man

Fig. 174.—Embryos of D. medinensis. (*From a microphotograph by Mr. H. B. Bristow.*)

in drinking-water, was digested; and that the parasite, being then set free, worked its way into the tissues of its new and definitive host; but all the experiments he made to bring about infection by means of ingestion of cyclops containing dracunculus larvæ gave a negative result. These failures led to the belief that the larva might have to undergo further changes before it was fitted for life in man. Considering the peculiar geographical limitations of this helminthiasis, and the very general distribution

Digitized by Google

of cyclops, such an arrangement seemed likely enough, though one German observer has stated that he succeeded in communicating guinea-worm to a monkey by applying living embryos to the skin of the animal.

Leiper has shown that when an infected cyclops is transferred to a 0·2-per-cent. solution of hydrochloric acid it is immediately killed, but the larvæ, so far from being destroyed, are aroused to great activity, and eventually escape into the fluid, in which they swim freely. From this he conjectured that under natural conditions man becomes infested through the ingestion of infested

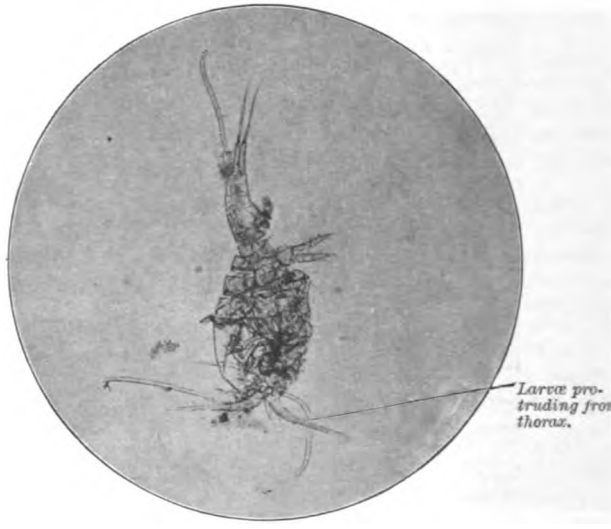


Fig. 175.—Embryos of D. medinensis in body cavity of cyclops.
(Photo: Mr. Andrew Pringle.)

The cyclops has been slightly compressed so as to force out some of the worms, which can be seen escaping from ruptures at the head and tail.

cyclops, the gastric juice acting on cyclops and larva in the same way as the hydrochloric acid in his experiment. In order to prove this he fed a monkey on bananas concealing cyclops which had been infested for five weeks, and which contained fully developed larvæ. Six months later, when the monkey died, five worms were found in its connective tissues, all possessing the anatomical characteristics of *D. medinensis*.

The evidence is now fairly complete that the life-span of the female dracunculus extends to about one year, conforming probably to the habits of certain species of cyclops which, under natural

Digitized by Google

conditions, serve as its intermediary host. It is not to be supposed that every species of cyclops is an effective intermediary; for, were this the case, guinea-worm infection would have a much wider geographical range.

Biological peculiarities explained.—The little that we now know of the life-history of the guinea-worm explains many things that were formerly mysterious. We now understand why the parasite, on attaining maturity, makes for the legs and feet; these are the parts of the human body most likely, in tropical countries, to come in contact with puddles of water, the medium in which cyclops—the intermediary host—lives. We can understand, also, why it is that the contact of water with the skin of the host causes the guinea-worm to expel her young; and we can understand the rationale of the douching so much practised by the natives of certain of the endemic districts in their attempts at extraction. The water-carriers in India are said to be very subject to guinea-worm, which, in their case, is prone to appear on the back—that is, the part of the body against which the water-skin lies when being carried. On this fact has been based an hypothesis that the young guinea-worm enters by the skin. One might interpret this fact, if fact it be, by suggesting that the mature guinea-worm, conformably to her instinct, seeks out that part of the body most in contact with water, which, in the case of the Indian water-carrier, is his back. In the mines of Nigeria it has also been noted that the worms migrate annually to the surface of the skin during the wet season.

Premature death of parasite.—Occasionally the guinea-worm fails to pierce the integument of her host; sometimes she dies before arriving at maturity. In either case she may give rise to abscess; or she may become cretified, and in this condition may be felt, years afterwards, as a hard convoluted cord under the skin, or be discovered only on dissection.

Habits.—The haunt of the female guinea-worm is the connective tissue of the limbs and trunk. When mature, and prompted by instinct, she proceeds to bore her way through this tissue, travelling downwards. In 85 per cent. of cases she presents in some part of the lower extremities. Occasionally she presents in the scrotum; rarely in the arms (Fig. 176); exceptionally in other parts of the body, or even in the head. In a proportion of cases the appearance of the worm at the surface of the body is preceded by slight fever and urticaria, as described by Sutherland in 1897 and by Bartet independently in 1898. Arrived at her destination she pierces the derma. Probably in consequence of some irritating

Digitized by Google

secretion, a small blister now forms and elevates the epidermis over the site of the hole in the derma. By and by the blister ruptures, disclosing a small superficial erosion $\frac{1}{2}$–$\frac{3}{4}$ in. in diameter. At the centre of the erosion, which sometimes quickly heals spontaneously, a minute hole, large enough to admit an ordinary probe, can be seen. Sometimes, when the blister ruptures, the head of the worm is seen protruding from this hole; as a rule, however, at first the worm does not show. If now we douche the neighbourhood of the ulcer with a stream of cold water expressed from a sponge and, as the water falls, watch the little

Fig. 176.—Female guinea-worm lying under the skin of the forearm. (*Orig.*)

hole in the centre of the erosion, we shall see in a few seconds a droplet of fluid—at first clear, later milky—well up through the hole and flow over the surface. Sometimes, instead of this fluid, a small, beautifully pellucid tube, about 1 mm. in diameter, doubtless the uterus of the worm prolapsed through her head parts, is projected through the hole in response to the stimulus of the cold water. When this tube has been extruded an inch or thereabouts, it suddenly fills with an opaque whitish material, ruptures and collapses, the fluid spreading over the surface of the erosion. If a little of the fluid, either that which has welled up through

Digitized by Google

the hole, or that which has escaped from the ruptured tube, is placed under the microscope, it is seen to contain myriads of dracunculus embryos lying coiled up, almost motionless, with their tails projecting in a very characteristic manner. (Fig. 174.) If now a drop of water be instilled below the cover-glass, the embryos may be observed to unroll themselves and, in a very short time, to swim about, *more suo*, with great activity. Manifestly, these embryos come from a guinea-worm lying in the tissues and communicating with the surface through the little hole in the derma. If the douching be repeated after an hour or longer, a further supply of embryos can be obtained; and this can be continued from time to time until the worm has emptied herself. Apparently the cold applied to the skin of the host stimulates the worm to contract and thereby force out her uterus, inch by inch, until it is completely expelled. When the protruded portion of uterus ruptures, under the pressure of the *vis a tergo*, it shrivels up, dries, and thus effectually seals up the end of that part of the organ which is still inside the worm, thereby preventing what might be inopportune and too prodigal discharge of embryos.

Diagnosis.—This is, as a rule, sufficiently obvious. Generally, if the worms cannot be seen they can be felt underneath the skin. In those cases in which both these methods fail, screening with the X-rays has been found to be of use (Dimier).

Treatment.—Formerly it was the custom, so soon as a guinea-worm showed herself, to attach the protruding part to a piece of wood and endeavour to wind her out by making a turn or two of this daily. Sometimes these attempts succeeded; just as often, the worm snapped under the strain. The consequences of this accident were often disastrous. Myriads of young escaped from the ruptured ends into the tissues, and violent inflammation and fever, followed by abscess and sloughing, ensued; weeks, or months perhaps, elapsed before the unhappy victims of this rough surgery were able to get about. Too often serious contractions and ankyloses from loss of tissue and inflammation, and even death from septic trouble, resulted.

If a guinea-worm be protected from injury, and the part she occupies frequently douched with water, her uterus will be gradually and naturally forced out inch by inch and emptied of embryos. Until this process is completed she resists extraction; possibly the hook at the end of her tail assists her to maintain her hold. When parturition, in from fifteen to twenty days, is completed, the worm is absorbed or tends to emerge spontaneously. A little traction, if practised then, may aid extrusion. Traction, however,

Digitized by Google

must not be employed so long as embryos are being emitted. The completion of parturition can be easily ascertained by the douching experiment already described.

Emily, a French naval surgeon, has introduced a system of managing guinea-worm cases which bids fair to shorten treatment and obviate the serious risks of the old winding-out system. By means of a Pravaz's syringe he injects the body of the worm, if she chances to be protruding, with solution of bichloride of mercury, 1 in 1,000. This kills the parasite; after twenty-four hours, extraction is usually easily effected. If the worm has not shown herself externally, but can be felt coiled up under the skin, he injects as near the coils as possible, and through several punctures, a few drops of the same solution. This, too, kills the parasite. Her body is then absorbed, as a piece of aseptic catgut would be, without inflammation or reaction of any description; or she may be cut down on, and easily extracted. Others have confirmed the value of Emily's method, which saves much time and suffering and, with due care, is devoid of risk. Chinosol 1 : 1,000 injected alongside the worm with a syringe has been practised in Nigeria with good effect; the worm dies in three days. Intravenous injections of tartar emetic have been given by Macfie in Accra in 23 cases, with very encouraging results. Apparently the drug is specific for the dracunculus, and a completed course of 3½–9 gr., given in 1-gr. doses on alternate days, is sufficient to cause the death of the worm and subsidence of the surrounding tissue reaction. According to Macfie's latest work, an injection of 4 gr. of antimony appears to be sufficient in most cases to kill both worm and embryos.

Prophylaxis.—From what has been stated with regard to the rôle of cyclops, it is evident that the prevention of guinea-worm is merely a question of protection of drinking-water from pollution by the subjects of guinea-worm infection. Leiper has shown that by raising by a few degrees the temperature of the water in which cyclops are living these crustaceans are killed. He suggests heating by a portable steam generator the water in wells and water-holes known to be sources of guinea-worm infection, as a prophylactic measure. Alcock has found that the addition of a trace of potash to the water is equally effective.

Digitized by Google

CHAPTER XLIII

PARASITES OF THE LUNG AND LIVER

I.—PARAGONIMIASIS (ENDEMIC HÆMOPTYSIS)

Paragonimus westermanni (Kerbert, 1878)

History.—This disease and the characteristic ova appearing in the sputum of the subjects were described by Baelz and Manson in 1880. Ringer, in 1881, was the first to find the mature parasite, which was afterwards described by Cobbold under the name *Distomum ringeri;* subsequently it was recognized to be identical with the previously described *Paragonimus westermanni* of the tiger. The main features of its life-history and pathological bearings have since been worked out by Japanese observers. Closely allied species are found in the pig, dog, cat, otter, and ichneumon.

Geographical distribution.—Endemic hæmoptysis occurs in China, Japan, Korea, Formosa, and the Philippines. In many of the endemic districts a notable percentage of the population is affected. It is not improbable that, as knowledge extends, the disease will be found to exist in other countries. The parasite which gives rise to this peculiar form of blood-spitting has been found in the United States in the cat, in the dog, and in the domesticated hog; ere long, therefore, we may hear of endemic hæmoptysis in man in America. The Chinese and Japanese are nowadays to be found in almost every land, and doubtless they carry with them their peculiar parasites—*Clonorchis sinensis*, *Fasciolopsis buski*, *Schistosoma japonicum*, and also *P. westermanni*. The establishment of these exotic species will depend, among other things, on their finding appropriate intermediary hosts.

Symptoms.—The symptoms generally begin so insidiously that it is impossible to fix their onset with accuracy. The subjects of endemic hæmoptysis have a chronic cough, which is usually most urgent in the morning on rising. The fits of coughing eventuate in the expulsion of a peculiar rusty-brown, pneumonic-like sputum. This sputum can be produced at will almost at any time, and often in considerable quantity. In addition to the chronic cough and the tenacious rusty expectoration referred to, the patient is liable to irregular attacks of hæmoptysis. Though

Digitized by Google

usually induced by violent exertion, occasionally such attacks come on without apparent cause. The hæmoptysis may be trifling; on the other hand, it may be so profuse as to threaten life—at all events, to cause intense anæmia. Ogi states that an outstanding physical sign in chronic cases is clubbed fingers.

The sputum.—On placing a minute portion of the viscid, pneumonic-like sputum under the microscope, its peculiar colour is found to be due partly to red blood-corpuscles, partly to a crowd of dark-brown, thick-shelled, operculated ova (Fig. 177). Besides pus-corpuscles there are large numbers of eosinophile cells.

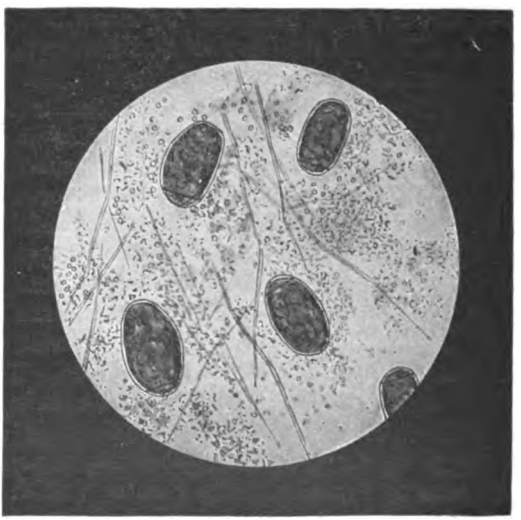


Fig. 177.—Ova of Paragonimus westermanni in sputum.

Charcot-Leyden crystals are often present. The ova vary a good deal in size and shape; they are all distinctly oval, have a yellow, smooth, double-outlined shell, and measure from 80 to 100 μ in length by 40 to 60 μ in breadth. If the sputum be shaken up in water, and the water be renewed from time to time, in the course of a month or six weeks—longer or shorter according to temperature—a ciliated miracidium is developed in each ovum. When the ovum is mature, on placing it on a slide and exercising slight pressure on the cover-glass the operculum will be forced back, and the miracidium will immediately emerge and begin to swim about and gyrate in the water.

Abdominal.—Abdominal symptoms may also be present;

Digitized by Google

they consist of dull abdominal pains and occasional diarrhœa. The abdominal wall feels hard to the touch and is tender; at the same time symptoms of liver cirrhosis, appendicitis, enlargement of the prostate, epididymitis, and adenitis may be present.

Cerebral.—When the disease affects the brain, epilepsy may be present for a considerable period, and may result in hemiplegia, aphasia, visual disturbances, pareses or monoplegias of various degrees.

Generalized.—In what is known as generalized paragonimiasis, in addition to the symptoms noted above, generalized lymphadenitis especially affecting the axillary and inguinal groups is present, and is associated with cutaneous ulcerations.

Pathological anatomy.—On making a section of the lungs in this disease, a larger or smaller number of what are known as "burrows" are discovered scattered about this organ, particularly towards the periphery. These burrows consist of areas, somewhat larger than a filbert, of infiltrated lung tissue in which can be seen a number of tunnels filled with the same material that constitutes the characteristic sputum, and also containing one, two, or more small trematodes. The septa between the tunnels may break down and a considerable cavity be thus produced; and as this occurs in connection with one of the bronchi, with which the tunnels always communicate, it may give rise to the appearance of a dilated bronchus. One burrow may communicate with another.

When first discovered it was supposed that *P. westermanni* was confined to the lungs. We now know that it may affect the liver, peritoneum, testes, intestine, skin, muscle, and brain. In the brain it forms a sort of tunnelled tumour similar to those in the lungs, and by the pressure or irritation proceeding from this tumour may give rise to a peculiar and ultimately fatal form of Jacksonian epilepsy.

Musgrave in his study of the pathology points out that the peculiar bluish, cyst-like burrows of the parasite occur in many organs and tissues. The infiltration of the tissues by the ova produces, especially in the serous membranes, little brownish-red patches sometimes visible to the naked eye. The intestinal mucosa is a common seat of infiltration when the ova give rise to inflammatory reaction, ending in ulceration and the appearance of ova in the fæces. Musgrave found no fewer than 100 mature parasites congregated in a psoas abscess.

The parasite.—The fluke is reddish-brown in colour, thick and fleshy, oval in shape, and measures 8–20 mm. in length by 5–9 mm. in breadth.

Digitized by Google

The cuticle is covered with broad, scale-like spines. Development of this parasite proceeds in a fresh-water snail, *Melania*, and thereafter the larva encysts in several species of fresh-water crab and crayfish living in rivers. For further details *see* Appendix II., p. 794.

Diagnosis.—Diagnosis of endemic hæmoptysis is at once established by the discovery of the characteristic ova in the almost equally characteristic sputum. Râles and other physical signs of lung consolidation are not usually discoverable. If the intestine or liver is implicated, ova may appear in the stools.

In the case of one-sided convulsions, or in hemiplegic affections occurring in a native of, or in a visitor from, the countries in which this trematode is endemic, the sputum should be examined on the chance of discovering evidence of the parasite. Should ova be found, there is a strong presumption that the cerebral trouble arises from a trematode tumour in the brain.

In the endemic zones of paragonimiasis, even in the absence of ova in the sputum, Musgrave recommends that this parasite should be suspected in cases of chronic epididymitis, enlargement of the lymph-glands or prostate, liver cirrhosis, and skin ulceration. As some of these conditions are also found in *S. japonicum* infestation, one should be careful to distinguish the operculated ova of paragonimus from those of the latter species. It is desirable that the sputum be examined bacteriologically to exclude the tubercle bacillus.

The cutaneous ulcerations have to be distinguished from those of oriental sore.

Ando has recently published a Bordet-Gengou test, using an extract of the body of the adult worm as antigen. This probably, when fully worked out, will constitute an efficient aid to diagnosis in obscure cases.

Treatment.—Hitherto no means of expelling the parasite from the lungs has been discovered. In the case of cerebral distomiasis it might be possible by an operation to remove the parasite and associated tumour, and thus afford a chance of recovery in what has hitherto proved a fatal condition. In consequence of the success of cumulative doses of tartar emetic, intravenously administered, in the treatment of schistosomiasis, there is reason to hope that this drug may be equally efficacious in paragonimiasis.

Prophylaxis in this, as in so many other animal parasitic diseases, lies principally in the direction of securing a pure water supply for drinking and bathing purposes, and avoiding all uncooked articles of diet, especially crabs and crayfish, which might

Digitized by Google

be supposed to contain the young parasites. The sputum should be destroyed.

II.—CLONORCHIASIS

Clonorchis sinensis (Cobbold, 1875)

Geographical distribution.—This disease has been found in many Eastern countries, including India, Mauritius, Japan, Korea, Formosa, China, and Tonkin. In the last-named country it appears to be very common. In Central Japan, according to Katsurada, there are certain districts in which it affects from 56 to 67 per cent. of the population.

The parasite.—*C. sinensis* measures 10 to 20 mm. in length by 2 to 5 mm. in breadth; it is oblong, narrow, flat, and somewhat pointed anteriorly, reddish in colour, and nearly transparent. Development outside the human body takes place in two different intermediary hosts, a mollusc, *Bythinia*, and in several species of fresh-water fish of the carp family. For further details *see* Appendix II., p. 790.

Pathogenesis.—*C. sinensis* inhabits the bile-ducts and gall-bladder. It thickens the biliary canals and expands them in places into cavities and diverticula as large as filberts. In these cavities vast numbers of parasites may be found. The diverticula communicate with the bile-ducts, along which the ova of the parasites, and sometimes the parasites themselves, escape into the intestine. The affected liver is enlarged as a whole, although the tissue in the immediate neighbourhood of the diseased bile-ducts is atrophied. The spleen, also, may be hypertrophied, and the intestine in a condition of chronic catarrh. Some instances are recorded of the presence of this trematode in the pancreatic ducts, in the duodenum, and in the stomach, and of the complication of ascites, and even anasarca.

This parasite, which for long was supposed to be practically innocuous, is now held to be the cause of a serious disease of the liver, which may terminate fatally; indeed there can be no doubt of this when one considers that in some of the cases recorded several thousand parasites were present. However, we should not overlook the possibility of complication and confusion with that other grave distomiasis of Japan and other Eastern countries, due to *Schistosoma japonicum*.

When the infestation is severe the liver becomes enlarged, and chronic diarrhœa, with recurring attacks of jaundice, sets in. Later, anasarca appears, and gradually a cachexia, resembling that of sheep-rot, is established, which, in the course of several years, may prove fatal.

Digitized by Google

Diagnosis.—It would be well to bear in mind this and other parasites in approaching the diagnosis of obscure hepatic disease associated with diarrhœa and jaundice in patients from the East. The discovery of the ova (Fig. 178) in the stools should guide to a correct diagnosis.

Treatment.—So far no specific treatment has been found. The patient should be removed to a non-infected area and given

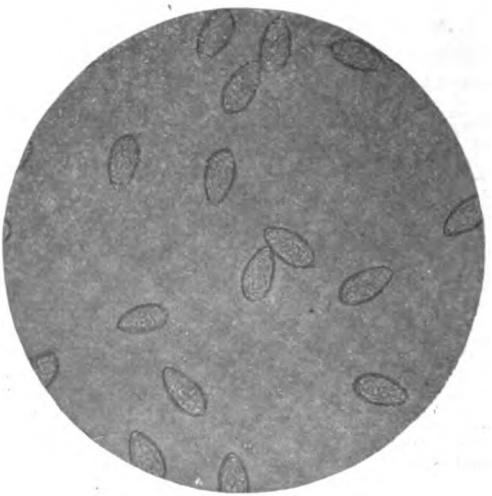


Fig. 178.—Ova of Clonorchis sinensis. × 250.
(*Microphoto: Dr. John Bell.*)

nourishing food. Recently salol has been reported as beneficial in the analogous liver-fluke disease of sheep. The parasiticidal action of intravenous tartar emetic upon the trematodes suggests a hopeful line of investigation in the treatment of this disease.

Prophylaxis.—Manifestly the Japanese habit of eating raw fish is to be deprecated. Animals and men harbouring the parasite should be prevented from fouling water—whether used for drinking or bathing, or for agricultural purposes.

Other and rarer trematodes which have been from time to time found in the human liver or gall-bladder are described in Appendix II., pp. 786-92.

Digitized by Google

CHAPTER XLIV

INTESTINAL PARASITES

Microscopical examination of the fæces for ova of intestinal parasites.—If the fæces of the natives of warm climates, and of Europeans coming from warm climates, are systematically examined with the microscope, in a large proportion of cases they will be found to contain the ova of one or other of three species of nematode worms—*Ascaris lumbricoides, Trichuris trichiura* (*T. dispar*), and *Ankylostoma duodenale*. The ova of the tapeworm and of the common thread-worm (*Oxyuris vermicularis*) are rarely found in the stools, as these parasites do not, as a rule, part with their ova until the joints of the former, or the entire body of the latter, have left the alimentary canal; but as the three nematodes first mentioned pass their eggs directly into the bowel, their eggs habitually appear in the fæces and constitute unequivocal evidence of the presence of their respective parental forms. Occasionally the ova of hepatic and intestinal parasites, such as *Schistosoma japonicum*, *S. mansoni*, *Clonorchis sinensis*, *Fasciola hepatica*, *Fasciolopsis buski*, and of rarer helminths, are encountered. (Fig. 181.) Without large experience the ova of the rarer parasites cannot be identified offhand; but if the practitioner has learned to recognize those of the three common species, he will at once know when he comes across the ova of any of the rarer species, and, on referring to some special work on helminthology, will have little difficulty in arriving at a correct diagnosis.

The microscopical examination of fæces for ova, though somewhat disagreeable, is by no means a difficult matter. All that is necessary, by way of preparation, is to place on the slide a minute portion of the suspected fæces—about the size of a hemp-seed—and then to apply the cover-glass, gently gliding it over the slide so as to spread out the mass in a thin, fairly uniform, and transparent layer. If the bit of fæces prove too consistent, a little water may be added so as to soften it. If the stools are loose and watery, the sediment should be taken up with a pipette and examined. It is well to make two or three preparations. The microscopical examination must, in the first instance, be made with a low power—an inch or, better, a half-inch objective. Search must be made in every part of the slide, and every suspicious body carefully scrutinized, a higher power being used if necessary. A very little practice suffices for the identification not only of the commoner ova, but of the species of parasite to which the ova belong.

The points to be attended to in the diagnosis of ova are size, shape, colour, thickness, roughness, smoothness, and markings on the surface of the shell; the presence or otherwise of yolk spheres, of a differentiated embryo, or, in the case of the cestodes, of the three pairs of embryonic hooklets; the existence of an operculum in the case of certain trematodes and of the broad tapeworms (*Dibothriocephalus*). The ova of the same species of parasite vary but slightly, and are in every instance sufficiently stable and definite for correct diagnosis.

Digitized by Google

Ova of Trichuris trichiura (Fig. 179, *c*).—Of the three common nematodes mentioned—*Trichuris trichiura, Ascaris lumbricoides,* and *Ankylostoma duodenale*—the ova of the first are the most frequently met with. They occur sometimes in enormous numbers, as many as six or eight specimens being visible in one field of an inch objective. They form a rather striking object

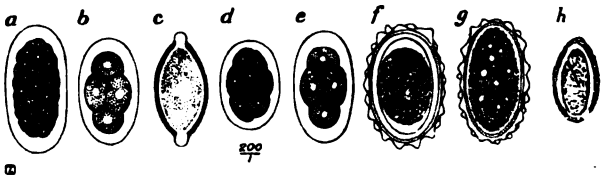


Fig. 179.—Ova of nematodes.

a, Trichostrongylus instabilis; *b*, Ankylostoma duodenale; *c*, Trichuris trichiura; *d*, Strongyloides stercoralis, found only rarely; *e*, Necator americanus; *f*, Ascaris lumbricoides; *g*, Ascaris lumbricoides (unfertilized); *h*, Oxyurus vermicularis.

under the microscope (Fig. 180). They are oval, measuring 51 to 54 μ by 21 to 23 μ, the ends of the long axis of the oval being slightly pointed and tipped with a little shining projection or plug. Their general appearance suggests an elongated oval tray, the projections at the poles of the ovum

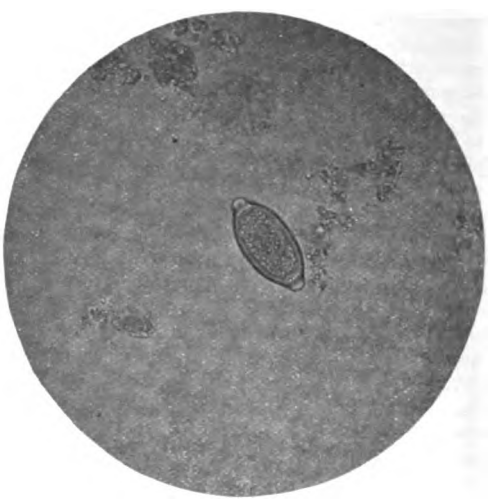


Fig. 180.—Ovum of Trichuris trichiura. × 250.
(*Microphoto: Dr. J. Bell.*)

representing the handles of the tray. They are dark brown in colour, sharply defined, doubly outlined, and contain no differentiated embryo.

The ova of *Ascaris lumbricoides* (Fig. 179, *f, g,* and Fig. 183) are considerably larger (60 to 75 μ by 40 to 58 μ) than those of trichuris (Fig. 179, *c*). They are also, as a rule, more spherical, or rather, more broadly oval; occasionally they are almost barrel-shaped. Like those of trichuris, they are

Digitized by Google

dark brown in colour from bile-staining, but they are much less sharply and smoothly defined, possessing a coarse thick shell which is roughened by many warty excrescences. The yolk contents are not always easily made out, nor, when made out, can any sign of embryo or segmentation be discovered. In certain instances, supposed to be unfertilized, the ova are smooth on the surface, the rough outer layer being almost or altogether absent.

A point of practical importance to be attended to lies in the circumstance that the rough outer layer on the shell of the ovum of ascaris is very easily

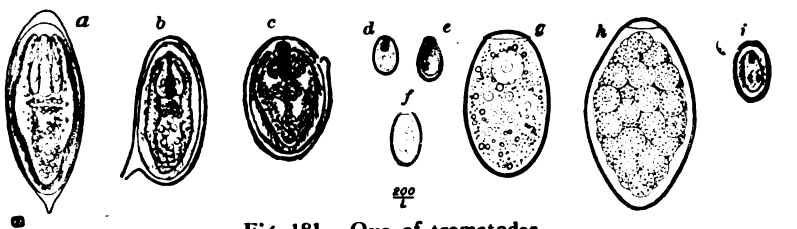


Fig. 181.—Ova of trematodes.

a, Schistosoma hæmatobium; *b*, S. mansoni; *c*, S. japonicum; *d*, Heterophyes heterophyes; *e*, Clonorchis sinensis; *f*, Opisthorchis noverca; *g*, Paragonimus westermanni; *h*, Fasciolopsis buski; *i*, Dicrocœlium dendriticum.

detached, leaving the egg with a sharp, smooth outline suggestive of some other species of parasite. To obviate this, in mounting fæces it is well to avoid too much gliding of the cover-glass over the slip.

The ova of *Ankylostoma duodenale* (Fig. 179, *b*) contrast very markedly with both the foregoing, particularly in the matter of colour. Trichuris and ascaris ova are invariably dark and bile-stained; those of the ankylostome are beautifully clear and transparent; they measure 55 μ to 65 μ by 32 μ to 43 μ; have a regular, somewhat elongated oval form, with a delicate, smooth, transparent shell, through which two, or four, or eight light-grey

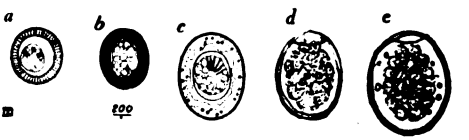


Fig. 182.—Ova of cestodes. (*After Looss.*)

a, Tænia solium; *b*, Tænia saginata; *c*, Hymenolepis nana; *d*, Dibothriocephalus latus; *e*, Diplogonoporus grandis.

yolk segments can be distinctly seen. It is well to search for these ova soon after the fæces have been passed; otherwise, owing to the rapidity with which, in favourable circumstances, development proceeds, the embryo may have quitted the shell and the egg be no longer visible.

The ova of the cestodes may be distinguished from those of the nematodes and trematodes by their circular outline, and, as a rule, by their smaller size.

The ova of *T. saginata* and *T. solium* are provided with a single brown-coloured striated outer membrane, which encloses a ciliated six-hooked onchosphere (Fig. 182, *a*, *b*). On the other hand, *Hymenolepis nana* ova have two transparent membranes (Fig. 182, *c*). Individual ova of *T. saginata*

Digitized by Google

are more ovoid in shape than those of *T. solium*; they measure 30 μ in diameter. The ova of *Dibothriocephalus latus* and *Diplogonoporus grandis* are translucent, oval in shape, and provided with an operculum (Fig. 182, *d*, *e*).

Nearly all intestinal ova are liable to become impacted in the human appendix; Risquey has published the detailed investigation of twenty-two appendices in which ova of *T. trichiura* were found nineteen times, *A. lumbricoides* four times, *Ankylostoma duodenale* twice, *Schistosoma mansoni* twice, and adult trichuris on two occasions.

For a description of substances which appear in the stool and may simulate ova of intestinal parasites, the reader is referred to Appendix III., p. 905.

Method of concentrating ova.—Clayton Lane has proposed a procedure called the "levitation method," which results in a tenfold concentration of

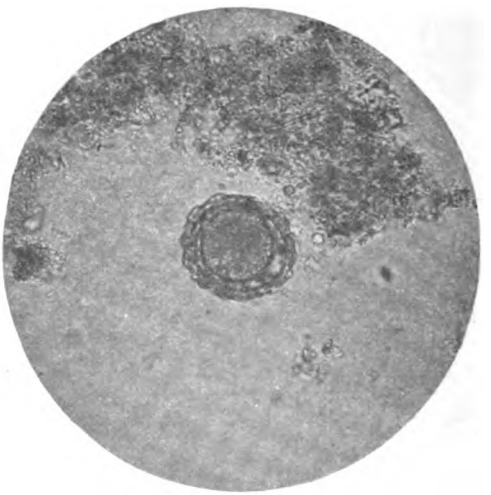


Fig. 183.—Ovum of A. lumbricoides. × 250.
(*Microphoto: Dr. J. Bell.*)

ova in a specimen of fæces. A measured ½ c.c. of fæces is transferred to a wide test-tube and as much water added as will fill the tube to four-fifths; it is thoroughly shaken, strained through wire gauze with a hundred mesh to the linear inch; the filtrate is then placed in a plain tube fitted at one end with a cork, and centrifuged. The sediment found on the cork when this is removed is washed on to a watch-glass. The methods of Bass, Garrison, Hall, and others are similar; the diluted fæces are passed through a silk screen, and the residue is treated and centrifuged with a fluid of a sp. gr. of 1047, consisting of citric acid 12 grm., water 86 c.c., formalin 0·2 grm.

Method of preserving ova.—For preserving ova in fæces Leiper recommends the following method: The fæces of a creamy consistency are mixed with lactophenol, which preserves the ova and destroys the fæcal odour. To any quantity of fluid fæces an equal quantity of Langeron's lactophenol is added; the whole is then intimately mixed by vigorous shaking. A permanent microscopic preparation can be made by stirring a small portion with a drop of glycerin and mixing with melted glycerin jelly. When this

Digitized by Google

is set the preparation is completed by sealing with gold-size. Langeron's lactophenol is made up of acid carbolic 1 part, lactic acid 1 part, glycerin 2 parts, water 1 part.

I.—NEMATODES

1. Ascariasis

Ascaris lumbricoides L., 1758*

Symptoms.—In many instances the ascaris gives rise to no very noticeable symptom; in other instances it is to be credited with a number of ill-defined gastric and perhaps nervous troubles —capricious appetite, foul breath, restless sleep, peevishness, vague abdominal pains, nausea, and so forth. It may cause urticaria of a most pronounced type. Sometimes the worms get into the stomach and are vomited, their appearance giving rise to no inconsiderable alarm. They may even creep up the œsophagus and into the mouth, or out by the nostrils. Cases are on record in which they caused suffocation by wandering into the rima glottidis. When aggregated into masses in the intestines they may cause a volvulus, and even intestinal obstruction. They have been known to enter the pancreatic ducts and also the bile-ducts and give rise to jaundice; to penetrate the intestinal wall and escape into the peritoneum, causing peritonitis; or to burrow into the abdominal walls and cause abscess. They may invade the lumen of the appendix and cause appendicitis, and their ova may occur in profusion in the latter situation. Fortunately these accidents are of rare occurrence; their possibility, however, should be borne in mind, and, apart from other obvious considerations, ought to make us endeavour to rid patients of these troublesome guests as soon as possible. With this object in view, it is well in certain countries, especially China and India, to give children, as a matter of routine, a few doses of santonin twice a year. Stewart's experiments on the life-history of *A. lumbricoides* have shown that the migrations of the larvæ through the pulmonary vessels cause an acute fatal pneumonia in pigs. It is possible that future research may show that pulmonary and urticarial symptoms may be produced in man also by this parasite.

Adults, especially young adults, although to a much smaller degree than children, are liable to entertain these verminous visitors. Sometimes certain obscure dyspeptic symptoms in grown-up people will resist all treatment until three or four grains

* For an account of the morphology and development of this parasite *see* Appendix II., p. 821.

Digitized by Google

of santonin and a purgative have been administered. Manson once had a patient who for a long time had been troubled with unaccountable nausea. One day, while he was sitting at breakfast, the feeling of sickness came on with unusual intensity. He had to leave the table, and, after one or two retching efforts, brought up an *Ascaris lumbricoides*. After this he was no more troubled with nausea. It is well, therefore, when puzzled over some obscure dyspeptic condition in tropical patients, to bear the ascaris in mind. If, for some reason, it is undesirable to give santonin unnecessarily, the stools ought first to be examined with the microscope. If ova (Fig. 179, *f*, *g*) are found, a dose or two of santonin may clear up the diagnosis and cure the patient; if no ova are found, the drug may be withheld and the idea of ascarides abandoned. The toxic symptoms produced by ascaris infestation are probably attributable to a substance known as *ascaron*, isolated by Shinamura and Fujii; it is a mixture of albumoses and peptones. When injected under the skin or intravenously it causes hyperæmia of all mucous surfaces, increased passage of urine and fæces, dyspnœa, œdema, palpitations, spasms, colic, rapid pulse, and urticaria. Larger doses may produce fatal results in experimental animals in from four to six hours. Using this substance as an antigen, positive complement-deviation results with the serums of horses that have been rendered immune to this substance are obtained.

Treatment.—The ascaris is readily expelled by a few grains of santonin. The dose is from ½ to 1 gr. for a child, 3 to 5 gr. for an adult. A good method of giving the drug is to prescribe three such doses on successive nights, the first and the last dose to be followed by castor oil next morning. Patients, or mothers, ought to be warned about the peculiar effect santonin has on the urine and sometimes on the vision. In his experience Manson only once saw any bad effect; in this instance a peculiar sort of intoxication, attended with delirium, which did not quite pass away for several days, followed its exhibition.

As a routine vermicide, oil of chenopodium, 5 c.c. made up with syrup, on three occasions, is, according to Darling and Barber, as efficacious as santonin; it also has the advantage of being specific for the ankylostomes, clonorchis, and tænia; even oxyuris and trichuris yield to this drug.

2. Ankylostomiasis

Ankylostoma duodenale (Dubini, 1843)

Definition.—A disease in its more pronounced forms characterized by great anæmia, debility, and cardiac incompetence, due

Digitized by Google

to the absorption of the toxins of *Ankylostoma duodenale* and *Necator americanus*, which inhabit the small intestine, and are sometimes present in enormous numbers.

Ascaris lumbricoides, though an unpleasant parasite, cannot be considered a dangerous one, unless in very exceptional circumstances. It is otherwise with the ankylostome; this, in many tropical countries, on account of the dangerous cachexia to which it gives rise, called ankylostomiasis, amounts to a positive curse.

Nomenclature.—The form of endemic anæmia with which these parasites are associated is of so marked a character that it has received a variety of distinctive names. Thus, in the French West Indies severe ankylostomiasis is known as *cachexie aqueuse*, sometimes as *malcœur*, or as *mal d'estomac des nègres;* in Colombia it is called *tuntun*, the sufferers being known as *tunientos;* in Brazil it has been called *oppilatio*, *opilacao*, and *cancaco;* in Europe it is sometimes known as "miner's anæmia" or "tunnel disease," the latter in allusion to the notorious St. Gothard epidemic; the form occurring in Egypt is spoken of as Egyptian chlorosis; in Ceylon it has been called "beriberi," a name which has not infrequently caused confusion with true beriberi; and, doubtless, elsewhere there are local names for this peculiar verminous anæmia.

History.—Although Griesinger had previously shown that Egyptian chlorosis was due to the presence of the ankylostoma in the small intestine, and although similar observations had been made on negroes in America, it was not until the very fatal epidemic of anæmia among the miners in the St. Gothard Tunnel (in 1880) had called the attention of European observers to the subject, that the importance of this parasite as a pathogenic agent began to be properly apprehended. Multiplied observations have now shown that, although very minute, these blood-sucking parasites, if present in large numbers and for a length of time, more especially if its victims are poorly fed, are very dangerous ones indeed. The constant drain of blood which their presence entails, the catarrh arising from the irritation caused by the wounds they inflict on the mucous membrane, the consequent impairment of nutrition, and, possibly, the absorption of some hæmolytic toxin—the product of the parasites—give rise to a grave cachexia, disqualifying to a greater or lesser extent the subject of it for work and, not infrequently, leading to a fatal issue. It is now recognized that many of the cases which were formerly regarded and diagnosed as "tropical anæmia" are cases of ankylostomiasis.

It is not in every instance in which the ankylostome is present that consequences so serious ensue. There may be dozens of

Digitized by Google

ankylostomes in the intestine without any appreciable anæmia, or, indeed, symptoms of any description whatsoever. Grave symptoms are the exception. One must be careful, therefore, to avoid concluding that the ankylostome is the cause of every pathological condition with which it may chance to concur.

On the other hand, many inhabitants of tropical and subtropical countries are in a state of chronic starvation. Living on coarse, bulky, innutritious food, they are prone to dilatation of the stomach and dyspeptic troubles. In such, any additional cause of malnutrition, as a swarm of ankylostomes, and a daily though perhaps small loss of blood, may be sufficient to turn the scale against them. In those countries, as elsewhere, there are many who live just on the borderland between health and disease; to such the ankylostome may prove "the last straw that breaks the camel's back."

It may be that in some persons with special susceptibility a toxin developed by the parasite produces a special type of anæmia, as in certain cases of *Dibothriocephalus latus* infestation.

It is evident that as a complication in typhoid, in kidney disease, in dysentery, in malaria, in fact in any chronic or exhausting disease, the importance of this anæmia-producing parasite cannot be ignored.

The practitioner in the tropics, therefore, must be constantly on the look-out in all cases of anæmia, of dyspepsia, and of debilitated conditions generally for the ankylostome. He must bear in mind that this parasite, as will be presently pointed out, if permitted to remain in the intestine for a length of time may be the cause, not only of remediable anæmia, but of irremediable anæmia-produced degenerations of various organs. On this account, also, its early recognition becomes a matter of the first importance.

Further, ankylostomiasis is an important disease from the standpoint of the employer of native labour. The invaliding and inefficiency which it causes among coolies, not to mention the deaths, are often financially a serious matter to the planter and the mine-owner. To them any wisely directed expense or trouble undertaken for the treatment and control of this helminthiasis will be abundantly repaid by the increased efficiency of the labourer.

Geographical distribution.—Since its discovery by Dubini, in 1838, the ankylostome has been found so widely diffused that it may be said to occur in all tropical and subtropical countries. It occurs in Belgium, and a few years ago was found by Haldane to be the cause of an epidemic of severe anæmia

Digitized by Google

in a Cornish mine. In northern countries it is rare; but it is abundantly present in the south of Europe, and in the tropical and subtropical regions of Asia and America. In Siam it occurs in 12 per cent. of the civilian prisoners, and is met with in South China in about 15 per cent. of the total population. It has been ascertained to exist in North and South Queensland, Australia, and in several of the islands of the Pacific. So prevalent is it in many parts of India that, according to Dobson, quite 75 per cent. of the inhabitants are affected. In Egypt it is found at nearly every post-mortem examination; and there the anæmia it gives rise to is one of the most common causes for the rejection of recruits for the army. Thornhill regarded its ravages in Ceylon as far more serious than those of cholera; this, not on account of the number of deaths it causes directly, but on account of the vast numbers affected, the chronic nature of the disease, and the aggregate mortality, direct, and especially indirect, for which it is responsible.

Fig. 184.—Ankylostoma duodenale. Natural size. (*Dubini.*) *a*, Male; *b*, female.

The parasite (Fig. 184).—The normal habitat of *A. duodenale* is the small intestine of man, particularly the jejunum, less so the duodenum, rarely the ileum or lower reaches of the alimentary canal; very occasionally it is found in the stomach. In these situations it attaches itself by means of its powerful buccal armature to the mucous membrane, from the blood of which it obtains a plentiful supply of nourishment. It is supposed to shift its hold from time to time, the abandoned bite continuing to ooze blood for a short period. It is said to be very prodigal of the blood it imbibes, the red corpuscles passing through its alimentary canal unchanged, the plasma alone being utilized.

The male and female ankylostomes—present generally in the proportion of one of the former to three of the latter—do not differ so much in size as is the case with many of the other nematodes. The male (Fig. 185) measures 8–11 mm. in length by 0·4–0·5 mm. in breadth; the female (Fig. 186), 10–13 mm. in length by 0·6 mm. in breadth. Both sexes are cylindrical in form, white when they are alive, grey when dead, reddish brown when full of blood. In both sexes the posterior end is the broadest part, whence the body tapers forwards to a narrow neck ending in a powerfully armed, bulging, and distinct mouth capsule. The margin of this remarkable organ is furnished with four strong, claw-like hooks—two on each side of the ventral line, and two conical teeth—one on each side of the dorsal line. The tail of the female is conical, ending in a short delicate spine; the anus is subterminal, and the vagina opens on the ventral surface at the beginning of the posterior third of the body. The tail of the male is provided with a large, umbrella-like, trilobate bursa possessing eleven ribs. Two long and very delicate spicules project from the cloaca, which opens at the bottom of the bursa. Owing to the relative positions of the sexual openings, the worms in conjugation look like the Greek γ.

Necator americanus closely resembles *A. duodenale*, but is shorter and

Digitized by Google

more slender (*see* Appendix II., p. 829). The male measures 2 mm. less than that species, and the female about the same amount. The buccal capsule is much smaller and contains a ventral pair of semilunar plates. Deeply situated in the same capsule are two pairs of lancets. The caudal bursa of the male appears to be divided into two. The two species may be distinguished by a naked-eye examination. In addition to being a smaller size, *N. americanus* has a peculiar dorso-ventral kink situated near the head. The eggs are slightly larger than those of *A. duodenale*. As in the case of the latter parasite, *N. americanus* inhabits the small intestine. The life-history of this worm is probably identical with that of *A. duodenale*. *N. americanus* has a wide tropical and subtropical distribution. At first it was thought to be confined to the American continent, but it has been found by Looss and others in pygmies from Central Africa, by others again in Rhodesia, India, Ceylon, Fiji, the Philippines, and elsewhere.

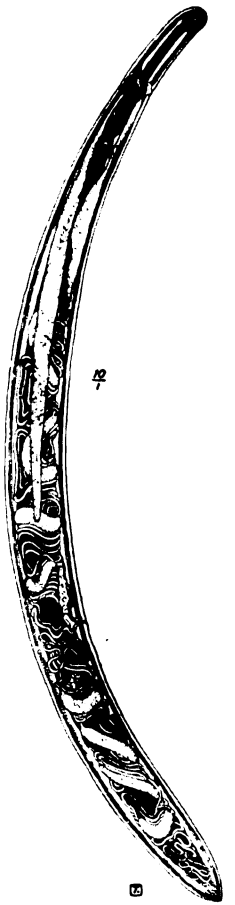


Fig. 185.—A. duodenale ♀. (*After Looss.*)

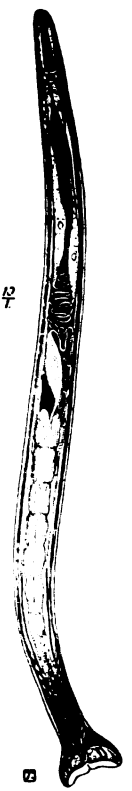


Fig. 186.—A. duodenale ♂.

Reproduction and mode of infection.—The female ankylostomes produce a prodigious and never-ending stream of eggs (Fig. 187), which pass out in the fæces. As already stated, while in the body of the host the development of the embryo does not advance very far; but on leaving the human host it proceeds, in suitable circumstances, so rapidly in the egg that in one or two days a rhabditiform embryo (0·2 mm. by 0·014 mm.) is born. (Figs. 188, 189). This minute organism (Fig. 190) is very active, voraciously devouring what organic matter it can find and, for a week, growing rapidly to 0·56 mm. by 0·024 mm. (Fig. 191). During this time it moults twice. After the second moulting it passes into a torpid condition, in which it ceases to eat, and growth is suspended. In this state it may

Digitized by Google

live for weeks or months, moving about more or less languidly in muddy water, in mud, or in damp earth. Should chance so determine, it is finally transferred to the human alimentary canal, either in muddy drinking-water, or in the mud or dirt adhering to the hands or the food dishes of the agriculturist, the brick-maker, or other operative engaged in handling the soil; or, it may be, in earth deliberately eaten by the geophagist and children. Arrived in its final host, after moulting again at the end of five weeks (Leichtenstern), it acquires sexual characters and the permanent adult form.

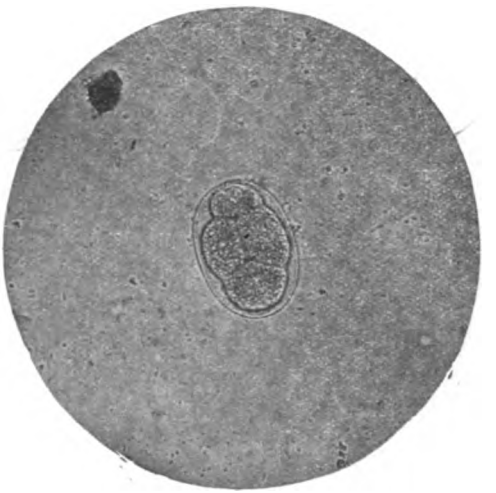


Fig. 187.—Ovum of A. duodenale. × 250.
(Microphoto: Dr. J. Bell.)

Until comparatively recently, this was believed to be the only method of infection, but Looss has shown that the parasite may reach the intestinal canal by another route. In making some experiments with "cultures" of ankylostoma larvæ, Looss inadvertently allowed the culture to come into contact with his hand. This was followed by redness and irritation of the skin of the part, and subsequently by well-marked ankylostomiasis, the sequence of events suggesting that the larvæ in the cultures had penetrated the skin of his hand and so attained the bowel. On another occasion Looss repeated this experiment on a human leg, an hour before its amputation. Sections of the skin showed the larvæ in the hair-follicles, and some had traversed the hair papillæ and lay in the connective tissue around the follicles.

Digitized by Google

Subsequently, other experiments on dogs and men established the fact that the embryos of *A. duodenale* can enter the skin, and that they do so as a first step towards reaching the intestine. From the subcutaneous tissue they enter the blood-vessels and lymphatics, and by this channel are passively transferred to the lungs. Here they leave the capillaries, enter the air vesicles, and thence along the bronchi and trachea pass into the œsophagus, and so to the stomach. It has been conjectured that during this passage the larva acquires the power of resisting the action of the gastric juice. If this be so, then the indirect route described must be the

Fig. 188.—Developing embryo in ovum of A. duodenale. × 250.
(*Microphoto: Dr. J. Bell.*)

only way by which the ankylostome can arrive at maturity. The success of feeding experiments, which hitherto has been regarded as proof that the parasite passed directly to the stomach, may be attributed to the passage of the larvæ into the wall of the œsophagus while the dose of larva-laden material was being swallowed.

Sambon suggested that a proportion of the ankylostoma larvæ pass directly, via the bloodstream, from skin to intestine. To test this suggestion, Fülleborn and Schilling-Torgau in one set of dogs divided the œsophagus, stitching the lower divided end to the skin; in another set of dogs a cannula was inserted into

Digitized by Google

the trachea so that the bronchial secretion could not pass into the œsophagus. The dogs were then infected with *A. caninum*. After a time both sets of dogs gave evidence of small-intestine infections of ankylostomes. Sambon's suggestion, therefore, is to some extent well founded.

The duration of the life of *A. duodenale* in the intestine has not been determined; some state it in months, others in years (Sonsino)—one to three. On account of liability to re-infestation, this point, an important one as affecting prognosis, is difficult to determine.

Fig. 189.—Embryo of A. duodenale escaping from ovum. × 250.
(*Microphoto: Dr. J. Bell.*)

Giles held that *A. duodenale* may become sexually mature while outside the human body and in the free state; in other words, that it is heterogenetic, an abundant supply of food favouring non-parasitic multiplication. His observations were opposed by Looss, who pointed out that probably other free-living nematodes had been mistaken for the species in question, and they are now merely of academic interest.

Symptoms. — The essential symptoms of ankylostomiasis are those of a progressive anæmia—an anæmia which is generally associated with dyspeptic trouble, but which, in uncomplicated cases, is not associated with wasting. If the progress of a case be unchecked, serous effusions in different organs and fatty

Digitized by Google

degeneration of the heart ensue, and death may occur from syncope or from intercurrent complication.

One of the earliest symptoms of an extensive ankylostome invasion is pain or uneasiness in the epigastrium. This is generally increased by pressure, but for the time may be relieved by food. The appetite, sometimes defective, is more often ravenous, though its gratification is apt to give rise to dyspeptic trouble of various kinds—to colic, to borborygmus, and perhaps to diarrhœa of imperfectly digested food. Constipation may be present in some instances, irregularity of the bowels in others. The taste may be perverted, some patients exhibiting and persistently gratifying an unnatural craving for such things as earth, mud, or lime—what is called *pica* or *geophagy*. The stools sometimes, though rarely, have a reddish-brown tinge from admixture of half-digested blood. Sometimes they may contain small flakes of blood-tinged mucus. Pure blood is rarely passed; and an extensive hæmorrhage, unless there be concurrent colitis, is still more rare, although, post mortem, considerable quantities of blood may be found in the small intestine. Fever of an irregular, intermitting, or even of a subcontinued type is common. On the other hand, the temperature may be constantly subnormal. Or these conditions may alternate. After a longer or shorter time, symptoms of profound anæmia gradually disclose themselves. The mucous surfaces and the skin become pallid, the face is puffy, and the feet and ankles are swollen. All the subjective symptoms of a definite anæmia now become more and more apparent; there are lassitude, breathlessness, palpitations, tinnitus, vertigo, dimness of sight, mental apathy and depression, liability to syncope, etc. The circulation is

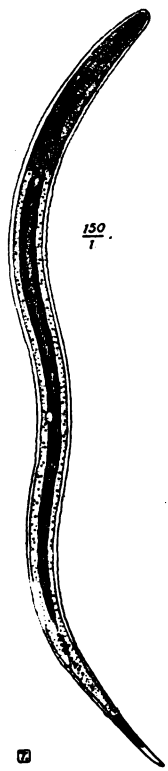


Fig. 190.—A. duodenale, mature larva.

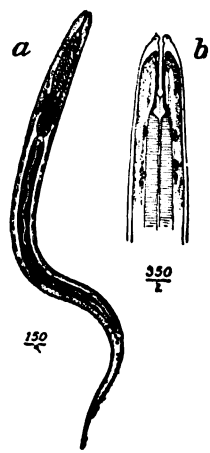


Fig. 191.—A. duodenale. *a*, Young larva; *b*, head.

(*Partly after Looss.*)

Digitized by Google

irritable, and hæmic bruits can be heard over the heart and larger blood-vessels. Ophthalmoscopic examination may reveal retinal hæmorrhages.

From some of these symptoms, were it not that with the advancing anæmia there is no loss of weight, one might be led to suspect the possibility of tuberculous or cancerous disease, or of Bright's disease. So far from losing weight, the patient may appear quite plump and, though hæmocytometric estimates testify to a slow and steady fall in the corpuscular richness of the blood until the lowest limit compatible with life is reached, there is no true poikilocytosis, as in idiopathic pernicious anæmia, no excessive leucocytosis, as in leucocythæmia, and not necessarily any enlargement of lymphatic glands, liver, or spleen. There is generally a marked eosinophilia of about 7–14 per cent. In rapidly fatal cases the eosinophiles disappear. The depression in the hæmoglobin value of the corpuscles is considerably greater than the fall in their number.

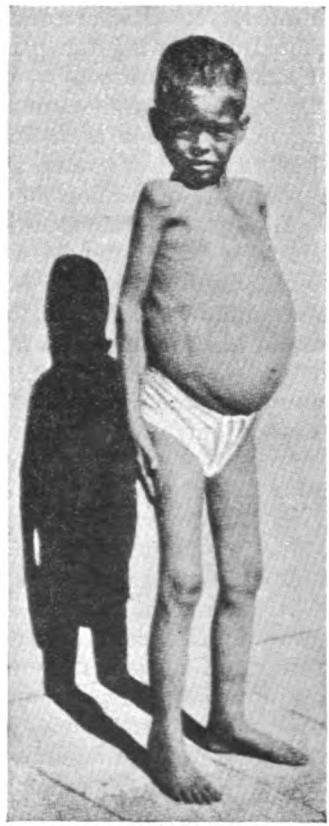


Fig. 192.—Ankylostomiasis in a South American Indian boy, showing stunted growth, characteristic facies, and protuberant abdomen. (*By permission of the Rockefeller Foundation.*)

The rate of progress is very different in different cases. In some a high degree of anæmia may be attained, and even a fatal issue, within a few weeks or months of the appearance of the first symptoms. Such rapid cases are rare; more frequently the disease is an exceedingly chronic one, ebbing and flowing or slowly progressing through a long series of years. Acute cases develop a terminal diarrhœa with passage of much mucus, and occasionally blood. These cases are apt to be mistaken for various forms of dysentery.

Should serious ankylostomiasis occur before puberty, the growth and development are apt to be delayed and stunted (Fig. 192).

Digitized by Google

There appears to be some reason for the belief that after generations of exposure to this infestation a certain degree of immunity is developed. Thus it is recounted that of the recruits chosen for Imperial service from St. Lucia during the Great War 67 per cent. of the first batch and 75 per cent. of the second were found infested, yet all were considered physically fit. This example is quoted as showing the partial immunity to the extreme ravages of ankylostomiasis enjoyed by the dark-skinned races. According to Darling, a given number of *A. duodenale* produce a greater degree of anæmia than an equal number of *N. americanus*. It is estimated that twelve worms are required to cause a loss of 1 per cent. of hæmoglobin.

Diagnosis.—Provided its presence be suspected, ankylostomiasis is easily diagnosed. In tropical countries, in patients coming from tropical countries, and in miners who work in very warm mines in cooler climates, anæmia with concurrent eosinophilia should always suggest a microscopical examination of the fæces. If the ova (Fig. 179, *b*, *e*, and Fig. 187) of *A. duodenale* or of *N. americanus* are discovered,* and no other reason for the anæmia is made out, the presumption is that one of these parasites is at the root of the mischief; at all events, no harm is likely to result from treatment based on this supposition. On the other hand, if no ova are found it must not be concluded that the case is not one of ankylostomiasis; for it sometimes happens that, in the later stages of the disease, symptoms will persist although the parasites which caused them in the first instance have disappeared spontaneously, or have been got rid of by treatment. The usual method of diagnosis by microscopic examination of stools for ova does not convey a quantitative idea of the severity of the infestation. The grade of infestation runs from one to a thousand or more worms. Diagnosis by means of a vermifuge is much the most satisfactory method; for instance, according to Darling, where the microscopic examination revealed a 75-per-cent. infesta-

* Bass considers that by the usual microscopical examination of fæces quite 20 per cent. of infections with *A. duodenale* are missed; he recommends examination of fæces as follows: "A quantity of fæces is well diluted with water, 1 to 10, and strained through gauze to get rid of coarse particles. It is then centrifuged and the fluid poured off, the centrifuge tube being refilled and centrifuged again until all the diluted fæces have been used. The precipitate is rewashed several times with water as long as anything can be washed out. Calcium chloride solution of a specific gravity of 1050 is now added, and the precipitate washed as before. This salt is preferable to others because of its hygroscopic properties, and its addition to the fæces disposes of everything having a specific gravity below 1050. The precipitate is now examined, and will be found to contain most of the eggs which were present in the whole amount of original fæces."

A more elaborate method, known as the *levitation method*, has been devised by Clayton Lane.

Digitized by Google

tion, diagnosis by vermifuge revealed an incidence of 97 to 100 per cent. Permanent degeneration of the alimentary canal, of the heart, liver, kidneys, and blood-forming organs, may remain, and even prove fatal, although the primary cause is no longer present. The history and the absence of other sources of anæmia are all we may have to go upon for diagnosis in such circumstances.

Ankylostomiasis is sometimes confounded with beriberi, and vice versa. The presence of paretic and cardiac symptoms not accounted for by the moderate degree of anæmia in beriberi, and their absence in ankylostomiasis, suffice for diagnosis. The anæmia of ankylostomiasis differs from that of malaria, inasmuch as the latter is accompanied by enlargement of the spleen, a sallow and perhaps pigmented complexion, an icteric tint of the scleræ, occasional attacks of well-marked periodic fever controlled by quinine, and, especially, the presence at such times of the malaria parasite in the blood. As an additional diagnostic feature, Rogers has pointed out that whereas in malaria the loss of hæmoglobin is in proportion to the loss of red blood-corpuscles, in ankylostomiasis it is in excess of this. Of course, ankylostomiasis and malarial cachexia may concur, and often do concur, in the same individual.

Ankylostomiasis very often occurs in association with pellagra, especially in the southern United States, and complicates the study of that puzzling disease.

In the East in general it may be associated with any form of diarrhœa. In Ceylon the Editor found the recognition of sprue in natives a matter of very real difficulty on account of this complication.

During the War a curious condition known as "war œdema," possibly identical with epidemic dropsy, occurred amongst the Turkish prisoners. In many features this œdema resembled that of ankylostomiasis, but could be distinguished by the absence from the stools of the characteristic ova, and of anæmia.

Some idea of the intensity of the infestation may be got from an enumeration of the eggs in a given quantity of fæces; according to Grassi and Parona, the presence of 150 to 180 eggs per cg. indicates an infection of about a thousand worms, male and female.

Morbid anatomy and pathology.—As already mentioned, the bodies of the victims of ankylostomiasis are not wasted; on the contrary, there is plenty of fat in the usual situations. The appearance of plumpness is further increased by a greater or lesser amount of general œdema. There may be effusions in one or more of the serous cavities. All the organs are anæmic. The heart

Digitized by Google

is dilated and flabby, its muscular tissue being in a state of pronounced fatty degeneration. The liver also is fatty, and so are the kidneys.

If the post-mortem examination be made within an hour or two of death, the ankylostomes, in numbers ranging from a few dozens up to many hundreds, will be found still attached by their mouths to the mucous surfaces of the lower part of the duodenum, of the jejunum, and perhaps of the upper part of the ileum; but if the examination has been delayed for some hours, the parasites will have dropped their hold, and are then to be found lying in the mucus coating the inner surface of the bowel. Many small extravasations of blood—some fresh, others of long standing—are seen in the mucous membrane, a minute wound in the centre of each extravasation representing the point at which a parasite had been attached. Sometimes blood-filled cavities, as large as filberts, are found in the mucosa; each cavity enclosing one or two worms and, probably, communicating by means of a small hole with the interior of the intestine. Old extravasations are indicated by punctiform pigmentations. There may be evidence, in the shape of vesiculations and thickening of the mucosa, of a greater or lesser degree of catarrh. Occasionally, streaks or large clots of blood are found in the lumen of the bowel.

Daniels and others report that microscopical examination of the liver and kidneys shows the presence, within the cells of the parenchyma, of grains of yellow pigment having the reactions of hæmatoidin—indicating an intravascular blood destruction such as occurs in pernicious anæmia and other diseases in which excessive hæmolysis is a feature. On this account, and also because he finds granules of a ferrous nature in the liver cells, Daniels concludes that the anæmia in ankylostomiasis is, in a measure, the result of blood destruction within the vessels by some toxic substance produced by the parasite and absorbed from the bowel. These results have not been confirmed by all other observers; on the contrary, the late Dr. Rake concluded, from careful estimates of the amount of iron in the livers of five cases of ankylostomiasis, that in this disease the hepatic iron is below the normal average, and that the anæmia is entirely owing to the direct abstraction of blood by the parasites. Further observations are necessary before this question can be decided.

Treatment. *Male fern.*—Until the introduction of thymol by Bozzolo, in 1880, extract of male fern was the anthelmintic usually employed in ankylostomiasis.

Thymol.—Before the administration of thymol the patient

Digitized by Google

should be put on liquid diet for a day or two, and have the bowels well cleared out by an aperient. In the morning, and following the action of the aperient, three or four 10- to 30-gr. doses of well-triturated thymol, in cachets, in capsules, or in emulsion, are given on an empty stomach at intervals of an hour. If the bowels do not open spontaneously within four or five hours of the last dose an aperient should be given. Usually, by this treatment many ankylostomes are expelled and may be found in the motions. One such course of thymol may suffice; but it is well, after a week has elapsed, again to examine the stools microscopically, and, if it be found that ova are still being passed, to repeat the course of thymol once or oftener.

Certain precautions have to be observed in employing this drug. At times it gives rise to a very unpleasant form of intoxication—vertigo, excitement, etc.—and the urine may become dark, as in carbolic-acid poisoning. It is advisable, therefore, for the patient, while taking the drug, to keep his bed and to lie down for several hours after the last dose. Thymol is very insoluble in water, and is consequently, in ordinary circumstances, not readily absorbed in poisonous quantities; should, however, the patient, while thymol is present in the stomach, partake of any alcoholic drink, there is considerable risk of poisoning ensuing. Alcohol, ether, glycerin, turpentine, chloroform, and oils are all solvents of thymol, and must therefore be avoided when this drug is being exhibited. Thornhill related an instance in which a fatal result was brought about, apparently, by neglect of the obvious precautions suggested by these facts. A man had received 30 gr. of thymol in water at 7 A.M. "He experienced no special symptoms after it, and at 9 A.M. the nurse gave him a second dose of 30 gr. As this man was supplied with arrack as an extra, and as in such cases a portion of the arrack was usually given at 9 A.M., the nurse gave it to him just after administering the second dose of thymol. The result was that intense collapse set in almost at once, and, notwithstanding all efforts, the man died within twenty-four hours, the collapse manifestly being due to the arrack dissolving the thymol, which was thus absorbed." Thornhill mentions two additional fatal cases of thymol poisoning occurring in his experience; other writers have recorded similar fatalities. For this reason, and because it is an extremely unpleasant drug to take—sometimes giving rise to severe burning sensations in the stomach, throat, and gullet, and not infrequently to excitement, giddiness, fainting, and vomiting—an equally efficient but safer drug is a desideratum.

Digitized by Google

The Rockefeller Commission advocate 60 gr. of thymol to be taken once a week till cured, preceded and followed by a saline purgative; the patient abstaining from food for eighteen hours during treatment. The minute directions given are as follows:—

(1) At 5 or 6 P.M. on the day preceding treatment a cathartic dose of sulphate of magnesia should be given. The patient should take no supper.

(2) He should remain in bed the following morning without food, and at 6 A.M. should take 30 gr. of thymol, and at 8 A.M. the remaining 30 gr.

(3) He should take a cathartic dose of sulphate of magnesia at 11 A.M. This should be repeated within two hours if a satisfactory movement of the bowels is not secured.

(4) No other food should be taken until after the bowels have moved thoroughly, and then all greasy food should be avoided.

(5) The usual diet may be resumed the day following the treatment.

(6) If a feeling of dizziness or weakness arises during treatment, half a cup of strong coffee should be taken.

(7) The thymol can be given in cachets, wafers, or capsules. The effects of the drug are increased by mixing with equal parts of lactose or sodium bicarbonate.

(8) The fæces should be re-examined at the end of seven days for worms or ova.

Without careful preparation by rest and judicious feeding, thymol must on no account be used in advanced cases of ankylostomiasis or where prostration is extreme. It is contraindicated in gastritis, dysentery, nephritis, and active heart disease.

When the maximum dose of thymol (30 gr. on three occasions) is given the Rockefeller Commission relate that 97·8 per cent. of the adult worms are removed.

Oleum chenopodii is reported to be more efficacious than thymol, less unpleasant to take, and less dangerous to the patient, with the additional advantage of being equally toxic to helminths other than the ankylostome. The maximum individual dose is 1 c.c. It may be given in three gelatin capsules containing ½ c.c. of the essential oil each, at two-hourly intervals, followed by ½ to 1 oz. of magnesium sulphate in three hours' time. Castor oil is not recommended. In either case it is found that 90 per cent. of the worms are removed. It is said that the administration of this drug is not entirely free from risk; dizziness and nerve inco-ordination have been reported as sequelæ. The drug has the advantage of being more uniform in its action than thymol, and of being less unpleasant to the taste, added to which it is only one-fifth the price.

Digitized by Google

Beta-naphthol given in the same way, in doses of 15 gr. repeated at intervals of two hours for two or three times, followed by a dose of salts, is nearly as efficacious, is cheaper and much less unpleasant, and is therefore to be preferred to thymol. It is, however, irritating to the kidneys, and hæmaturia is reported to have followed its administration.

Oil of eucalyptus 30 minims, chloroform 45 minims, castor oil 10 drachms, one half first thing in the morning, the other half thirty minutes later, is a very efficient vermifuge in ankylostomiasis, much less unpleasant and much less dangerous than any of the foregoing. It can be repeated for several days in succession. Manson used this combination several times in Europeans who had on previous occasions taken thymol; they preferred the eucalyptus mixture. The dose of chloroform is a large one, and chemists may hesitate to dispense it, but, in our experience, it has never had any ill effects.

A daily dose of 5 gr. of thymol, kept up for several weeks, has been advocated by some practitioners of experience and might be tried in those cases of ankylostomiasis in which more drastic treatment is contraindicated by a condition of extreme debility.

The reports on various anthelmintics used in the hookworm campaign by the Rockefeller Commission show that *N. americanus* is much less resistant than *A. duodenale*, and for the latter species it is urged that oil of chenopodium is much more efficacious than thymol, beta-naphthol, or oil of eucalyptus.

Convalescence.—The dieting of convalescents from serious ankylostome disease must, for a time, be very carefully conducted. In such cases a rich, full dietary is to be avoided until the powers of digestion have become re-established; otherwise, enteritis and diarrhœa may prove very troublesome and retard recovery—perhaps prevent it altogether. Iron and arsenic are indicated as blood restorers.

Prophylaxis.—In devising a system of prophylaxis for ankylostomiasis, the fact that it is by means of the fæces of the already infected that the parasite is spread must be kept prominently in view. Fæcal contamination of the soil and water must therefore be prevented. The promiscuous deposition of fæces about huts, villages, and fields must be interdicted. Abundant and easily accessible privy accommodation must be provided in coolie lines, in miners' camps, in native villages, and along the highways of traffic. In the absence of a more elaborate system of conservancy, pits or trenches will suffice. They may be filled up with earth, and fresh ones opened from time to time. The Chinese plan of

Digitized by Google

storing night-soil for months in large cemented, water-tight pits is a good one. It is known that if the ova of the ankylostome are kept in pure fæces the embryo is developed and escapes from the eggs in due course; but it is also known that unless the embryo be supplied with a certain amount of air and earth it soon dies. The thing to be avoided, therefore, is the mixing of *fresh* fæces with earth. By the Chinese system the embryos of the ankylostome are killed, and, at the same time, a valuable fertilizer is secured for the agriculturist.

It is manifest that in devising privies and sanitary regulations the habits of the people they are intended to benefit must be taken into account; if this be not attended to, if native habits and prejudices are ignored, any system, no matter how perfect it may be in theory, will fail in practice.

The water supply should also be carefully guarded from all possible sources of fæcal contamination. Drinking-water, unless above suspicion, should be boiled or strained. So far as possible, facilities for removing all earth and mud from the hands and dishes before food is partaken of should also be provided and their use encouraged.

Badly contaminated ground had better be abandoned. If this should be found impracticable, the soil should be turned over with the plough, or roasted with grass fires, or treated in such a manner that any ova or embryos it may contain are destroyed or buried. The systematic periodical inspection of plantation coolies is to be recommended. At these inspections all subjects of anæmia or dyspepsia should be put aside for more careful examination; if the ova of ankylostomes are found in their fæces a judicious dosing with some of the drugs mentioned may avert serious disease in the individual, and also prevent him from becoming a source of danger to his companions.

In view of the great danger to health that exists in certain countries from this and similar parasites, the sanitary authorities in such places ought to circulate among the people, by means of printed leaflets or posters, a few simple directions for the prevention of ankylostomiasis and kindred diseases. Nicoll has recommended common salt as a prophylactic agent of some potency. It has the advantages of being cheap and generally easily obtainable. It has an injurious effect upon the larvæ, but requires to be brought into very intimate contact; mere sprinkling is futile. Solid salt, however, when sprinkled on fæces does not penetrate the mass for forty-eight hours.

Attempts have been made in Porto Rico and elsewhere to reduce

Digitized by Google

or exterminate the prevailing ankylostomiasis. Special officers have been detailed for the purpose, whose duty it is to submit the entire population to systematic drugging with beta-naphthol. The result in the improvement of the general health and increase in the aggregate labour capacity has been most encouraging. This is an example of sanitary energy which we might follow with advantage in our own tropical possessions. Clayton Lane estimates that out of 315 million inhabitants of British India, 45 million wage-earners are subjects of ankylostomiasis. Employers of labour in the Darjeeling district estimate that the labourer's earning capacity when freed from this disease is increased by 25–50 per cent.

A campaign against the hookworm—as the ankylostome is called in America—is now being waged in the United States, financed by Mr. Rockefeller. State and county dispensaries for free examination and treatment of applicants have been established. The total number treated in 11 States in 1912 was 238,755; a Commission has been working for three years, and has treated 393,556 people at a cost of a little over a dollar per head. The reports issued by the Commission contain most valuable statistics, of which a few may be quoted. In Panama, in 1916, 30,094 persons were examined, and 80·4 per cent. found infested; of these 98·2 per cent. received first treatment, and 49·9 per cent. were cured. In Antigua, of the total population, 98·8 per cent. were examined, and 29·8 per cent. found to be infested. Treatment was meted out to 92 per cent. of the infested people, and 96 per cent. of these were cured. In British Guiana, out of 3,900 infested natives, only 8·6 per cent. remained as foci of infestation at the end of the campaign. In Ceylon, of 4,567 tea plantation coolies, no less than 95·6 per cent. were found infested.

All persons now travelling through St. Lucia are required to produce a certificate to show that they are free from hookworm disease.

Darling recommends that, as the agricultural and mining population within the tropics is so universally infested with hookworm, the detection of individual infestations by microscopic examination is no longer necessary. The population should therefore be treated *en masse* by an intensive method.

ANKYLOSTOME DERMATITIS

A form of dermatitis affecting the feet of coolies on plantations in Assam, in the West Indies, and probably elsewhere in the tropics, and variously known as ground itch, pani-ghao, water itch, water

Digitized by Google

pox, water sores, sore feet of coolies, has been ascribed by Bentley to the penetration of the skin by ankylostome larvæ. The disease is of much economic importance to the planter.

The soil in the neighbourhood of coolie lines is extensively contaminated by fæcal matter. During rainy weather the ankylostome ova in the fæcal materials are hatched, and the larvæ escape into, and possibly multiply in, the damp earth. The bare feet of the coolies are constantly soiled with this larva-laden earth; and, in this way, in many tropical plantations, Looss's experiment is unintentionally carried out on a large scale. Dermatitis, vesiculation, and it may be pustulation or even extensive ulceration, and probably ankylostomiasis anæmia, ensue. The services of the affected coolie are lost to the planter till the irritation subsides and the anæmia is cured.

Bentley's suggestion has been contradicted by Dalgetty, Stiles, and others. Looss also points out that the symptoms of ground itch do not tally with those caused by the penetration of ankylostome larvæ through the skin. Perhaps coolie itch may not in every instance be produced in this way, but undoubtedly it is so in a proportion of cases. A patient of Manson's, a sugar planter, who at that time knew nothing about the ankylostome, observed that an attack of coolie itch in any of his labourers was sure to be followed by anæmia. He assumed that the skin trouble was the cause of the anæmia, and that the former was produced by a micro-organism picked up from the soil. He made his coolies, on going out to their work in the morning, walk through a bucket of Barbadoes tar, and then through a heap of sand, with the result that coolie itch and anæmia ceased on his estate.

Personal cleanliness and the use of some form of foot-covering during the wet season, together with the prophylactic measures for ankylostomiasis already mentioned, are the special preventive measures indicated as against this disease. As regards treatment, antiseptic foot-baths and some soothing ointment are indicated.

II.—CESTODES

The ordinary tapeworms, *Tænia saginata* and *Tænia solium*, and their cystic forms, are common enough in the tropics and subtropics, their distribution being regulated by the presence or absence of their proper intermediary hosts—the ox in the one case, the pig in the other—and by the habits of the people as regards cooking and conservancy. *Echinococcus granulosus* (= *Tænia echinococcus*) of the dog, and its cystic form—hydatids—are found wherever the dog and the sheep are found, that is practically

Digitized by Google

everywhere. The broad tapeworm (*Dibothriocephalus latus*) is known to occur in Turkestan, in Japan (where the natives are in the habit of eating raw fish), in Madagascar, and among the natives on the shores of Lake 'Ngami, South Africa. Ichthyophagous habits are probably responsible for the occurrence of *Diplogonoporus grandis*, another large dibothriocephalid found by Ijima and Kurimoto in a Japanese from the province of Higen.

The only cestodes of man which, so far as is known, have any claim to be regarded as more or less special to warm climates are *Hymenolepis nana*, *Davainea madagascarensis*, *D. asiatica*, *Sparganum mansoni*, and *S. proliferum*. Doubtless there are other species which, so far, have escaped observation.

Treatment.—Special care should be devoted to the preparation of the patient for anthelmintic treatment. Aperients, either castor oil or salts, should be taken to clear out the bowel for two days beforehand, and the diet restricted to light food. *Filix mas*, or extract of male fern, much the most reliable drug in cestode infestations, in an ethereal extract, should be taken early in the morning of the fourth day. The dose is 1 dr., and is repeated in an hour; the patient must then remain quiet and take a dose of salts an hour or more later. Should the head not appear in the motion which is passed, Manson found the eucalyptus, chloroform, castor oil mixture (p. 673) most efficacious if given immediately after the final aperient. Powdered pomegranate bark 3 oz., macerated in 10 oz. of water, has a considerable reputation among native races as an anthelmintic.

III.—INTESTINAL MYIASIS

A residence in the alimentary canal of some vertebrate animal is a regular feature in the life-history of many dipterous insects. The ova of the insect are either licked from the skin or swallowed in the food on which they had been deposited. In this way they get transferred to the stomach, where, after a time, the larvæ are hatched out and undergo development. In due course they appear in the fæces. Man is not infrequently victimized in this way, especially in tropical countries. Sometimes, until a correct diagnosis is arrived at, not a little alarm is caused by the appearance of these creatures in the stools. They are easily recognized. The ringed, cylindrical body, from ½ to 1 in. in length according to species, broad at one end, tapering at the other, and usually beset with little spines or hairs, is sufficiently diagnostic. (Fig. 193.)

Already we know over twenty species of diptera whose larvæ have been found in or expelled from the human intestinal canal.

Digitized by Google

In Europe the majority of cases of intestinal myiasis, a not infrequent occurrence, are caused by *Fannia canicularis* (a fly closely resembling the common housefly and erroneously considered a young form of the latter on account of its smaller size), and the closely related *F. scalaris*. Austen believes that intestinal myiasis, due to the larvæ of these flies, is probably to be traced to the

Fig. 193.—Larva of Calliphora vomitoria.

parent flies having oviposited on the anus when the patient has been using some country privy where such insects are common.

A dose of castor oil will probably suffice to expel any of these creatures that may not have been passed spontaneously.

A rational prophylaxis would consist in the covering up of food after it has been cooked, in order to prevent the access of flies.

Instances in which the larvæ have been discharged per urethram have also been met with, though more rarely.

Digitized by Google

Section VI.—DISEASES DUE TO POISONS, INCLUDING SNAKE-BITE

CHAPTER XLV

VEGETABLE POISONS

AN exhaustive account of the various poisonous plants, their uses and antidotes, is beyond the scope of the present volume. All that can be done is to indicate those of most importance to the tropical practitioner.

ARROW POISONS

The arrow poisons employed by native races vary. Some owe their toxicity to micro-organisms such as the tetanus bacillus, others are plant poisons, whilst a third group is obtained from the poisonous secretions of coleopterous larvæ and from snake venom.

The arrow poisons of African tribes are derived from poisonous plants of the genera Acocanthera, Strophanthus, and Adenium. Of these the first-named genus is the most important; it supplies the arrow poisons used by the East, West, and Central African tribes. They are small shrubs with white or red flowers and violet-tinted fruits. A decoction of the wood is evaporated down to a thick tar-like mass, the poison. The active principle is a powerful cardiac depressant causing heart-failure. The strophanthus poison, used in the Congo, Lake Nyasa, and the Gold Coast, is obtained from decoctions of the seeds of that plant; death takes place through cardiac failure. In South-West Africa the natives extract a poison from the sap of *Adenium bœhmianum*, of which the active principle is *eckujin*; this also probably exerts a virulent cardiac effect. The pygmies of the forest use a substance obtained from *Erythrophlœum guineense* mixed with strychnine, while the Waigogo of East Africa employ the sap of *Euphorbia candelabrum*. The Hottentots of South Africa were in the habit of extracting an active and irritating principle from the larva of a cockchafer, *Diamphidia locusta*, which causes a considerable amount of œdema and cutaneous inflammation.

In Asia arrow poisons are still in use in Malaya, Sumatra, and Borneo, and are prepared from various species of Aconite, Antiaris, and Strychnos. In Malaya the upas tree, *Antiaris toxicaria*, provides arrow and dart poisons, of which the active principle is *antiarin*, obtained from the inspissated juice of the tree, and which in many ways acts like digitalis; it is called *ipoh* or *ternek*.

In Borneo and Malacca poisons are derived from *Strychnos tieuté*, and are known as *aker lampong*; they contain both strychnine and curare, and produce acute respiratory failure.

South American arrow poisons are all obtained from various species

Digitized by Google

of Strychnos, of which the active principle is *curare*; they produce acute respiratory paralysis by action on the motor nerve-endings.

The general treatment of a poisoned-arrow wound should be directed towards preventing absorption of the poison by applying a bandage above the site of the wound. If, owing to the barbs, the arrow-head cannot readily be removed at the site of entry, the best method consists in thrusting the head through the skin on the opposite side of the limb. After withdrawing it, the wound must be thoroughly washed out with a 5-per-cent. solution of potassium permanganate; cardiac action must be maintained by means of stimulants; if strychnine has been used in the first instance, morphia should be given as an antidote.

POISONS USED FOR CRIMINAL PURPOSES

Of inorganic poisons, the one most generally used by tropical races is arsenic in some form, cleverly intermingled, as a rule, with flour, or even inserted into the grains of maize or millet, or introduced into sweets as in Egypt. Native races usually possess a much wider and more intimate knowledge of organic poisons than do civilized peoples.

In Brazil common native poisons are derived from *Paullinia pinnata*, which contains an alkaloid, *timboin*, and from the fruit of *Thevetia ahonai*, of which the active principle is *thevetosin*; both of these excite vomiting and cause respiratory failure.

In the Dutch East Indies a poison extracted from the roots of *Milletia seriacea* is employed, which produces debility, headache, diarrhœa, collapse, and death.

In the Pacific islands the native poison is obtained from the fruit of *Barringtonia speciosa*.

In India a large number of vegetable poisons are in use. In the Madras and Bombay Presidencies an extract is obtained from the roots of *Nerium odorum*, the white oleander, which contains two glucosides having a specific action on the heart. Similar substances, *urechitin* and *urechitoxin*, derived from *Urechites suberecta*, exert a cumulative action, and therefore sudden death may take place in the victim without suspicion of poisoning being aroused.

The juice of an *Asclepias* is used in India as an infanticide; the symptoms induced are vomiting, salivation, and cramps. The roots of various species of Aconite (*A. ferox*, etc.) are used for the same purpose; death is said to take place rapidly—in three to six hours, as a rule. Several species of Apocynaceæ, such as *Cerbera odollam* and *Thevetia neriifolia*, the sap and seeds of which contain a glucoside, *thevetin*, are very deadly—death from cardiac failure taking place in from twelve to fifteen hours. In Southern India, Burma, and Ceylon a decoction of the fruit of the *Gloriosa superba*, one of the Liliaceæ, allied to squills, is employed for criminal and suicidal purposes. The active principle, *superbin*, causes gastro-intestinal irritation and cardiac failure within four hours. The commonest poison in India and Ceylon is the datura, one of the deadly nightshades, of which there are several species. The seeds, mixed with food or drink, produce a state of extreme mental exaltation followed by coma; the active principles are *atropine*, *hyoscyamine*, and *scopolamine*.

In Central Africa the leaves of *Hyoscyamus fahezlez*, containing hyoscyamine and scopolamine as active principles, are used by the Tuaregs of the Sahara. On the West Coast a decoction of a cactus, colloquially known

Digitized by Google

as *oro*, produces blisters in the mouth, vomiting and gastro-intestinal irritation, collapse, and death within a few hours.

DISEASES DUE TO THE INGESTION OF POISONOUS FOODS

Lathyrism

This disease, characterized by various nervous manifestations such as ataxy, spastic paraplegia, weakness, and muscular pains, without any psychical disturbances, occurs in Abyssinia, Algeria, and India in those districts in which vetches, *Lathyrus sativus* and allied species, form the main article of diet. A similar disease occurs in animals fed upon the same food. The arms and trunk are seldom involved; incontinence of urine and sexual impotence are early and common symptoms. The disease is a very chronic one and seldom ends fatally.

Atriplicism

A combination of curious cutaneous and nervous symptoms is known in China under this name. It is an intoxication caused by the ingestion of the leaves of *Atriplex littoralis*. The earliest symptoms consist of great itching of the hands, followed by œdema, and often by blebs and bullæ as well; the finger-tips may become gangrenous, cutaneous hæmorrhages may occur, and the face and eyelids become cyanotic and œdematous. In many ways the condition resembles Raynaud's disease and erythromelalgia.

Ackee Poisoning (Vomiting Sickness of Jamaica)

An acute and very fatal condition locally termed "the vomiting sickness" has been known for many years in Jamaica. It is found principally in rural districts and occurring in what were regarded as circumscribed epidemics. Until quite recently its causation and nature were neither apprehended nor understood, although several Commissions had attempted their elucidation. To Dr. Harold Scott belongs the merit of clearing up the mystery, and indicating simple and practicable methods of prevention, which, if given effect to, must avert a considerable mortality, particularly among children. It is estimated that since 1886 over 5,000 lives have been lost in Jamaica from this cause alone.

The vomiting sickness is confined to the West India Islands, and practically to Jamaica, and occurs principally during the cooler months—November to April.

Symptoms.—A previously healthy child suddenly complains of abdominal discomfort, vomits several times, and apparently recovers, perhaps falling asleep. Three or four hours later, vomiting—now of a cerebral type—recurs. Within a very short time, a few minutes perhaps, convulsions and coma supervene; and death follows, on an average about twelve hours from the oncoming of the initial vomiting, though it may occur in as short a period as one and a half hours. The case-mortality amounts to 80–90 per cent. In those who recover, convalescence is complete in twenty-four hours.

During the attack the temperature is normal or subnormal, rarely rising to 101°; the pulse is 90 to 100; the respirations are 26 to 30, sometimes, as death approaches, being of the Cheyne-Stokes type. The pupils are slightly dilated and, until near the end, react to light, etc. Unless during the convulsive seizures, there is no muscular rigidity. Post-mortem examination reveals hyperæmia of viscera with a tendency to minute interstitial

Digitized by Google

hæmorrhages, together with marked fatty changes, especially in the liver and kidneys, and sometimes to a less degree in the pancreas and heart-muscle.

Etiology.—Scott has shown, on what must be regarded as convincing evidence—clinical, seasonal, epidemiological, and experimental—that the vomiting sickness is really the result of poisoning by a fruit, much used by negroes in Jamaica, called *ackee*, the fruit of *Blighia sapida* (Fig. 194), a tree very common in the island. When mature and in good condition this fruit is wholesome enough; if gathered before it is quite ripe and before it has opened while on the tree, or if gathered from an injured branch, or opened after falling on the ground, it is poisonous. It would appear that the poisonous element in the immature and unsound fruit is soluble in water, for the "pot water" in which the ackees have been cooked is much more toxic than the cooked fruit; and, further, that the poison is precipitated by alcohol.

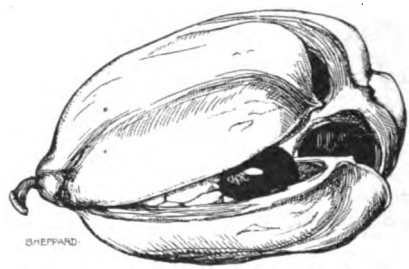


Fig. 194.—Ackee fruit (Blighia sapida). Half nat. size. (*Wellcome Bur. Sci. Res.*)

Treatment.—An emetic, and washing out the stomach with an alcoholic fluid during the primary vomiting, seem to be indicated. Scott is insistent that the administration of alcohol must be prompt; it precipitates the poison.

Prophylaxis.—When the fruit in various stages falls to the ground, only the opened pods should be used for food. The immature unopened pods should all be destroyed.

Alcoholism and Drug Habits

Alcohol poisoning occurs in varying degrees among nearly all native races, and in its symptoms and course does not differ materially from alcoholism in other parts of the world. Rum (65–72 per cent. of alcohol), obtained from the fermentation of molasses, is used in the West Indies and South America; arrack (50–60 per cent. alcohol) is manufactured in India, China, and Java from fermented rice or palm sap; while a slightly fermented drink known as toddy is obtained from sweet sap of various palms, and is drunk in India, Ceylon, and West Africa. In South America a potent alcoholic drink is made of the fermented juice of *Agave americana*, and is known as "pulque."

Opium poisoning.—The opium habit, either as eating or as smoking—the symptoms of which are too well known to require description—is common throughout the tropics. Opium poisoning is also a favourite form of suicide of women.

Cannabis indica, Indian hemp, or *hascheesch*, grows in India, Persia, and Arabia, and is a variety of the common hemp, *Cannabis sativa*. The

Digitized by Google

leaves are powdered down, and either chewed or smoked as a preparation known as *bhang ;* an extract of the flowers is known as *ganga.* Both these preparations cause a state of great nervous excitement and, if persistently used, often lead to permanent insanity, the main features of which are hallucinations and illusions. Hascheesch in its various preparations, often with the addition of extracts of various Solanaceæ, such as datura and nux vomica, is habitually taken daily by millions of the inhabitants of Africa and Asia.

The most stringent Government regulations have been framed with a view to suppressing this trade.

Kawa or **Yangona**, the powdered root of one of the Piperaceæ, prepared so as to form a beverage, is drunk on festive occasions throughout Polynesia. Formerly the root was masticated by specially selected girls previous to the final steps in the preparation of the drink ; this practice was a prolific source of tuberculosis, and was on that account prohibited. Over-indulgence in *kawa* produces a state of hyperexcitement, with loss of power in the legs. Chronic intoxication produces a condition of debility, with coarse roughened skin.

Betel.—The chewing of betel, the leaves of *Piper betel*, together with lime and areca nut (*Areca catechu*), is a common practice in India and Ceylon and generally throughout the East ; the mouth and lips are stained a bright-red colour. In Central Africa the nuts of the kola tree (*Sterculia sp.*) are chewed habitually, and act as a muscular stimulant without, it is said, producing any detrimental effects.

Digitized by Google

CHAPTER XLVI

ANIMAL POISONS

SNAKE POISON AND SNAKE-BITE

THE anatomy and classification of snakes are dealt with in Appendix II., p. 872; the best-known and most dangerous species are there described. Here it suffices to say that whilst vipers or adders are the only poisonous snakes found in Europe, the very deadly colubrine snakes abound in Asia—e.g. the cobra, *Naja tripudians*, the king cobra, *N. bungarus*, and the kraits, *Bungarus cæruleus* and *B. fasciatus* (Figs. 195, 196)—besides the most poisonous viperines, the daboia, *Vipera russellii*, and the phoorsa, *Echis carinatus* (Figs. 197, 198). In the American continent are found the most important poisonous viperines of the family *Crotalinæ*, to which the rattlesnakes, *Crotalus terrificus* (Fig. 199), *C. scutulatus*, *C. durissus*, and *C. horridus*, the copperhead, *Ancistrodon contortrix*, and the moccasin, *A. piscivorus*, belong. In South America are found various species of *Lachesis*, of which *L. lanceolatus* (Fig. 200), the "fer de lance," is the best-known, and the colubrine *Elaps corallinus*, the dreaded coral snake of the West Indies and British Guiana. North Africa possesses a species of cobra, *Naja haja*, and two vipers, *Cerastes cornutus* and *Echis carinata*; in the south of that continent another species of cobra, *Naja flava*, and two vipers, *Causus rhombeatus* and *Bitis arietans*, the puff adder, are found. Australia and Tasmania possess a large number of venomous colubrines, amongst which may be mentioned the "death adder," *Acanthophis antarcticus*, the tiger-snake, *Notechis scutatus*, the copperhead, *Denisonia superba*, the brown snake, *Diemenia textilis*, and the black snake, *Hotechis pseudechis*.

The sea-snakes found in the Pacific and Indian Oceans, the *Hydrophinæ*, are all poisonous, with one exception—*Platurus*. They live entirely in water and have flattened tails adapted for that habitat.

In snakes the poison is secreted by symmetrically placed racemose glands analogous to the parotid and salivary glands of vertebrates, and is ejected through a duct which traverses the poison fang.

Digitized by Google

The venoms vary very greatly in degree of toxicity, and especially in their lethal action on different species of animals ; the most poisonous are those of *Notechis scutatus*, the Australian tiger-snake, and the Indian sea-snake, *Enhydrina valakadien*. The amount

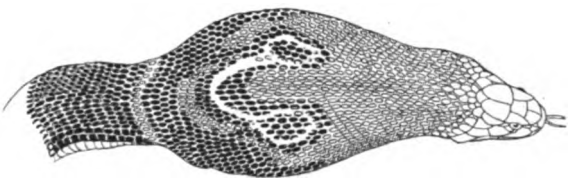


Fig. 195.—The king cobra (Naja tripudians).

varies considerably in different species—e.g. *Naja tripudians*, the cobra, secretes about 1 c.c. of venom containing about 370 mg. of solid matter ; it is a clear, straw-coloured fluid, acid in

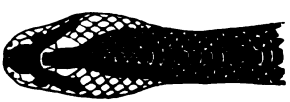


Fig. 196.—The krait (Bungarus fasciatus).

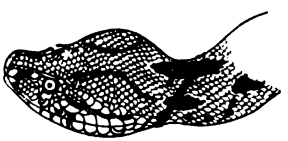


Fig. 197.—The daboia (Vipera russellii).

reaction, and when in a dried state retains its toxicity almost indefinitely.

The specific action of the venoms appears to depend upon the

Fig. 198.—The phoorsa (Echis carinatus).

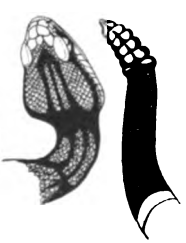


Fig. 199.—Rattlesnake (Crotalus terrificus).

Fig. 200.—Lachesis lanceolatus.

ferments and lysins they contain. As far as is known, the following substances enter into their composition, viz. fibrin ferments, proteolytic ferments, cytolysins acting upon red cells, leucocytes, epithelial and nerve cells ; agglutinins, and neurotoxins, with

Digitized by Google

affinity for all nervous tissue, and especially for the respiratory centre. The neurotoxins preponderate in the venom of the colubrines, while those which act upon the blood and cardio-vascular system are most characteristic of the viperines; in the Australian colubrines both classes of toxins may be found.

Symptoms of snake-bite in man.—The physiological action and symptoms produced by snake venoms can be classified into two groups, the colubrine and the viperine.

1. *Colubrine.*—In the case of cobra-bite there is severe pain in the part, which soon becomes inflamed and œdematous. After an interval of an hour the patient becomes dull, apathetic, and unable to stand. Nausea and vomiting, with profuse salivation and paralysis of the tongue and larynx, supervene. Soon the respiratory centre becomes involved and respiration ceases. Should the patient survive the paralytic symptoms, recovery is rapid. The pupil is contracted throughout.

The bite of the krait *Bungarus cæruleus* is extremely dangerous, especially in Northern India; the symptoms are similar to those produced by the cobra.

The symptoms caused by the bite of the Australian colubrines may not be very severe, but the constitutional effects appear with great rapidity—sometimes in as short a period as fifteen minutes. A feeling of faintness and an irresistible desire to sleep are soon followed by paresis of both legs, vomiting, and cardiac paralysis. The pupil is widely dilated and insensible to light. Should the patient survive the coma, recovery is complete and no sequelæ occur.

2. *Viperine.*—As the type of lesion produced by the viperines, that of Russell's viper, *Daboia russellii*, may be described. This species is extremely deadly; the bite causes severe pain with rapidly forming and extensive œdema, together with blood-stained discharge and ecchymoses around the site of the punctures. Collapse, small thready pulse, nausea and vomiting, dilated pupils insensitive to light, soon supervene, together with a loss of consciousness more or less complete, from which a temporary recovery sometimes occurs. Should the effects of the now diffused toxin wear off, the local condition of the wound becomes aggravated; extensive local suppuration and sloughing, malignant œdema, or even tetanus and hæmorrhages from the mucous surfaces—hæmaturia melæna—may occur. There is no paralysis or other symptom pointing to implication of the central nervous system. Viperine venom is less resistant to heat and more easily destroyed by caustic agents than colubrine venom.

Digitized by Google

The bite of *Echis carinatus* is less dangerous than that of the daboia, but is in many ways similar in its effects.

The bites of the rattlesnakes, *Crotalus*, are remarkable for the degree of local disturbance they produce. Constitutional paralytic symptoms come on quickly, usually in less than fifteen minutes. Should the patient recover from this state, the swelling and discoloration extend up the limb and trunk, and general symptoms of blood poisoning, with pyrexia, restlessness, and delirium, set in. The wound itself suppurates freely and may become hæmorrhagic or even gangrenous. The symptoms produced by the bite of the European vipers resemble those of crotalus, but in a very much lower degree.

The mortality from snake-bite, even of the most venomous varieties, is not so great as it is popularly supposed to be; it is estimated at about 30 per cent. That it should not be more is probably due to the fact that, unlike what takes place in experimental animals, the reptile is seldom able to inject a full dose of venom. If given a fair chance, the cobra is able to inject no less than the equivalent of twenty lethal doses at a time.

Treatment of snake-bite.—To be effective, all treatment should be vigorously and promptly applied. It should be directed, firstly, to prevent absorption of the poison; secondly, to neutralize, as far as possible, its toxic effects. A ligature should be tied around the limb immediately above the bite; for this purpose, if it is at hand, a stout indiarubber band, firmly applied, is the best ligature. In the case of the colubrines this probably has little or no effect in preventing the absorption of the neurotoxins; but in the case of the viperines it is, no doubt, very effective in so far that it localizes the fibrin ferments, causes extensive intravascular clotting in the bitten part, prevents the process from becoming generalized, and affords time for the action of other remedies.

Amputation of the part above the bite has been proved to be effective if performed *immediately*.

The next steps must be directed towards destroying the poisons remaining at the site of injection. This is best effected by freely incising the bite in the direction of the lymphatic and venous circulation. The wound should then be well swabbed out with a strong solution of permanganate of potash; this destroys any toxin with which it comes in contact. Some advocate the rubbing in of crystals of the same substance. Acton and Knowles have lately advocated the injection of 10–20 c.c. of a 5-per-cent.

Digitized by Google

solution of gold chloride in ox-bile as being an improvement upon potassium permanganate.

Contrary to the popular idea, sucking the wound is useless.

Alcohol and strychnine were formerly regarded by some as antidotes, but are now known to have no efficacy whatsoever.

Serum treatment.—It has long been known that immunity could be produced in animals by repeated and progressive inoculation of venom; a similar result is produced in men who have been repeatedly bitten by snakes of one species. This immunity, however, is specific only for the venom of the particular species. Calmette attempted to produce in *antivenene* a serum which should be active against all snake venoms, but his claim to have done so has not been substantiated.

The serum prepared against cobra venom is found to be antitoxic to the homologous venom, and to a certain extent to that of *Bungarus fasciatus*, but is without action on the viperine venoms daboia, echis, lachesis, and crotalus. The serum produced against daboia venom has no action whatever upon the venoms of naja, bungarus, etc.

In practice one encounters the very great drawback that only the antiserum specific as to the snake concerned will be of use in a given case of snake-bite. The only practical method of meeting this unfortunate circumstance is to issue an antiserum effective against the most common and most dangerous snakes in any given country. All antivenenes are relatively weak in their action as compared to antidiphtheritic and antitetanic serums. The antivenene should be injected in large amounts and as soon after the bite as possible. Acton and Knowles have demonstrated that such a serum must be given before the minimum lethal dose of venom has been absorbed, and that it requires no less than ten minutes to find its way into the circulation. The injection should be done *intravenously*, and at least 100 c.c. should be given. In India the serum treatment, if available, should be employed in every case on the chance that the snake was either a cobra or a daboia.

There is still much work to be done before an efficient polyvalent serum can be obtained. One of the difficulties in arriving at this is that every injection of venom into the horse for the production of immunity gives rise to abscess-formation, and that the whole process of preparation lasts from a year to a year and a half.

Other measures.—Little else can be done except to keep the patient warm. Small doses of alcohol, ammonia, and strychnine should be given as stimulants, but the practice of exhibiting almost

Digitized by Google

poisonous doses of alcohol cannot be too strongly deprecated. Rogers has advocated, on physiological grounds, the employment of adrenalin in those snake-bites in which the toxins have a marked paralytic action upon the vaso-motor centres. Acton and Knowles have advocated artificial respiration in colubrine poisoning.

For further information on this important subject the reader is referred to more exhaustive treatises, especially the article by Profs. Calmette and Bruyant in Mense's "Tropenkrankheiten," 2nd edit.; Martin and Lamb's article in Allbutt and Rolleston's "System of Medicine;" Fayrer's "Thanatophidia of India;" contributions by R. H. Elliot and Sir T. Fraser in *Philosoph. Trans.*, Royal Soc., 1904 and 1905; Acton and Knowles, *Indian Journ. of Med. Research*, 1914, 1915, etc.

Poisonous Lizards

Many lizards are unjustly suspected of being injurious to man. Two species, however, are known to secrete a venomous substance. One, *Heloderma horridum*, is a denizen of Mexico, especially of the hot dry slopes of the Cordilleras in the neighbourhood of Tehuantepec. This reptile may reach a length of 5 ft. or more. The poison it secretes is introduced by its bite and is much dreaded by the natives. In many respects the symptoms it produces resemble those of cobra venom, but in a milder degree. The other poisonous species, *Lygosoma sundevalli*, a jumping lizard, indigenous to South-West Africa, secretes a poisonous substance in its skin which is thought to be injurious to man.

Poisonous Fishes

Poisonous fishes exist in most tropical waters, especially among the coral reefs of the Pacific and Indian Oceans. Their venom may be conveyed to man either through their bite or by means of poisonous stings. In the first instance the poison is secreted by certain epithelial glands within the mouth; in the second, by means of poison-glands connected with barbs in the dorsal fin. The first of these classes comprises more than one hundred species of the genus *Muræna*, all of which possess powerful teeth capable of inflicting bites. (Fig. 201.) The poison secreted by the glands courses down the teeth, which are hollowed for the purpose. The effect of the venom on man is neuro-cardiac. The second class contains a great number of widely separated genera. In some the poison finds its way to the exterior only when the barbs are broken, and produces severe inflammation in the wound, and it may be tetanic symptoms. *Synanceia*, a spinous species, is widely distributed throughout the Indian and Pacific Oceans;

Digitized by Google

Plotosus anguillaris, known as "machoira" in Mauritius, has a similarly wide distribution; while a coral-living species, *Saccobranchus fossilis*, in the waters of India and Ceylon, produces similar symptoms.

In South American waters several species of *Thalassophryne* have similar dorsal spines containing a central poison-duct connecting with the glands. Species of *Trachinus* found in northern waters, as well as in the Mediterranean, have two sets of poison barbs,

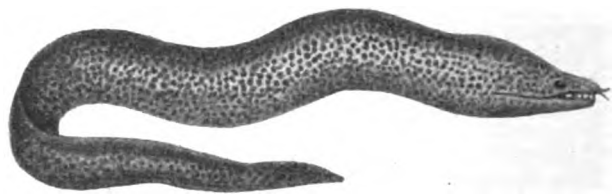


Fig. 201.—Muræna moronga. (*After Calmette.*)

on the operculum as well as on the dorsal fin. The venom has a general action on the heart, besides the purely local effect.

Many species, over forty in all, of *Scorpæna* are found in tropical waters; their integument is provided with numerous rays, the stings of which may excite convulsions and even cause death.

Scorpions and Spiders (Arachnida)

Scorpions are very common in the tropics, and their stings are very painful and cause a considerable amount of inconvenience, though they are not exactly dangerous, except to young children, in whom, in addition to local symptoms, muscular cramps, profuse perspiration, pyrexia, vomiting, and convulsions may be produced. Deaths have been reported from North and South Africa, the West Indies, Mexico, Korea, and Manchuria.

In Southern Europe and North Africa the black scorpions, *Euscorpius italicus* and *Buthus maurus*, in Mexico a species known as the "durango" (*Centrurus*), in Manchuria *Buthus martensi*, are specially dreaded. (Fig. 202.)

The paired poison-glands are situated in the last or postanal segment of the tail, which is jointed and very flexible, so that it can be curved forwards over the body when the scorpion is striking. The venom which it ejects is in many respects like that of the cobra, but, of course, is by no means so toxic.

The *treatment* for scorpion-sting is based upon the same principles as that for snake-bite. A ligature is first applied, and

Digitized by Google

the wound is incised and well washed out with a strong solution of potassium permanganate. Impressed by the number of deaths among children in Upper Egypt attributed to scorpions, Todd has produced an efficient antitoxin. The venom extracted from the dried stings and venom-glands by means of normal saline is toxic to the horse, goat, and most laboratory animals, while the desert fauna, such as the desert rat, the jerboa, the fennec fox, and hedgehog, are immune. The antitoxin has been prepared from horses by subcutaneous injection of graduated doses of venom. In doses of 5 c.c. it exerts both a prophylactic and a curative action.

Spiders.—Nearly all spiders (*Araneæ*) possess poison-glands, the venom of which is injurious to insects, but only a few species are dangerous to man. Certain species of the genus *Latrodectus* are believed to be very poisonous. In New Zealand one species, *L. hasselti*, known as the "katipo," in Southern Europe *L. tredecimguttatus*, the "malmignatte" (Fig. 203), and in North and South America three, *L. mactans*, *L. curacaviensis*, and *L. geometricus*, occur.

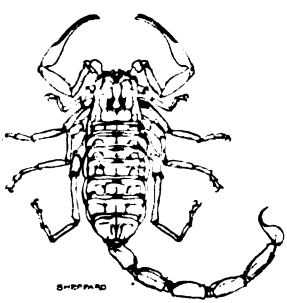


Fig. 202.—Scorpion (Buthus sp.). Half nat. size.

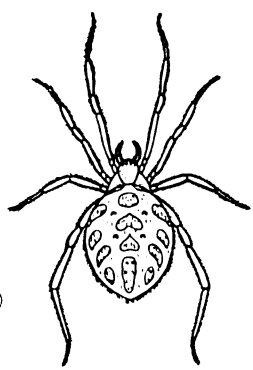


Fig. 203. — Latrodectus 13-guttatus. × 2. (*After Hirst, "Journ. Economic Biol."*)

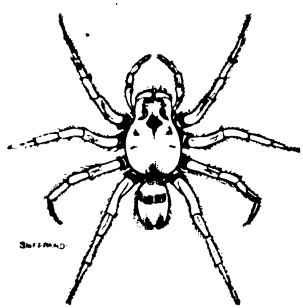


Fig. 204.—Lycosa tarentula. Half nat. size.

The toxin of the poison-glands has been shown to be a powerful hæmolysin, causing inflammation and œdema at the site of injection, together with numbness of the part, and, it may be, an urticarial rash. Escomel has noted even more serious symptoms in children, such as jaundice and hæmoglobinuria. Sloughing of the skin in the neighbourhood of the bite may occur. *Treatment* consists in washing out the wound with a solution of potassium

Digitized by Google

permanganate (1 : 4,000), and its internal administration in doses of one teaspoonful every two hours.

In Peru a pruning spider, *Glyptocranium gasteracanthoides*, which lives in the leaves of vines, and is identified by its ash-grey colour and large globular abdomen with two prominent tubercles, produces, according to Escomel, the same symptoms as *Latrodectus*, and sometimes hæmaturia.

The true "tarantula" spider, *Lycosa tarentula* (Fig. 204), occurs in Southern Europe. Mysterious properties have been attributed to its bite; apparently in some specially susceptible people œdema of the eyelids and pyrexia are apt to result. The so-called tarantulas of tropical countries are bird-eating spiders belonging to the family Mygale. They are trap-door spiders, terrestrial in their habits, with prominent projecting mandibles which give them a terrifying appearance. The North African species, *Chætopelma olivacea*, is much feared by the Arabs; its bite is said to give rise to acute inflammation.

Centipedes (Myriapoda)

The Chilopoda, to which the poisonous genus *Scolopendra* belongs, are widely distributed in the tropics. They are large species, and possess a poison apparatus at the base of the first pair of appendages, which are modified so as to form jaws. The tropical species, *Scolopendra morsitans*, reaches a large size, up to 6 in.; the venom causes both local and general symptoms. The site of the bite becomes inflamed and the starting-point of a lymphangitis; dizziness, headache, and vomiting may ensue. *Treatment* consists in bathing the part with a strong solution of ammonia, 1 : 5 or 1 : 10. It may be necessary to give hypodermic injection of morphia to allay the pain.

Digitized by Google

Section VII.—TROPICAL SKIN DISEASES

CHAPTER XLVII

NON-SPECIFIC, BACTERIAL, FUNGOUS DISEASES, ETC.

I.—NON-SPECIFIC SKIN DISEASES

Prickly Heat

Prickly Heat, or, as it is sometimes called, lichen tropicus, is probably a form of miliaria (not of lichen) connected with the excessive sweating incident to the heat of tropical climates. According to Pollitzer, the mechanism of its production depends on the non-cornification of the cells of the stratum corneum, the individual cells of which, in consequence of their being sodden by constant perspiration, swell and so obstruct the orifices of the sweat-glands, thereby leading to accumulation of sweat in the ducts. Pearse regards the disease as an acute distension of the sebaceous glands by their own secretion; the glands, he holds, are over-stimulated in order to supply an adequate amount of sebum to the skin, so as to make up for the loss of that material washed away by inordinate sweating. Durham described a small amœba in the skin lesions, but this has not been confirmed.

Nearly every European in the tropics suffers from prickly heat, particularly during the earlier years of residence. Some never seem to become acclimatized in this respect, but continue year after year to exhibit their crop of prickly-heat lesions when the hot season comes round.

Though sufficiently annoying in the robust and healthy, in them prickly heat is not a grave affair. It is otherwise in the case of the invalid, of delicate sickly children, of hysterical and, especially, of parturient women; to these it may prove, by interfering with sleep and provoking restlessness, a very serious matter. Prickly heat is also a common though indirect cause of boils; for the breaches of surface, following on the scratching it induces, afford many opportunities for the invasion of the micro-organisms of furuncular disease.

Prickly heat consists of a miliary-like eruption, generally most profuse on those parts of the body, as around the waist, which are closely covered with clothing; but it also occurs on the backs

Digitized by Google

of the hands, the arms, legs, forehead, occasionally on the face, the scalp, in fact on any part of the surface of the body except the palms and soles. The minute, shining, glass-like vesicles, and the numerous, closely set, slightly inflamed papules, give the skin the feeling as if thickly sprinkled with grains of sand. The eruption may keep out for months on end, becoming better or worse according to circumstances. The pricking and itching are often exceedingly distressing. Anything leading to perspiration immediately provokes an outburst of this almost intolerable itching—nothing more certainly than a cup of hot tea or a plate of hot soup. Long drinks, exposure to the hot sun, close rooms, warm clothing, all aggravate the distress. Sometimes the little vesicles may pustulate, doubtless from micrococcus infection. So soon as the weather becomes cool the eruption and the irritation quickly subside.

Treatment.—Manifestly the most important thing is the avoidance of all causes of perspiration—particularly the copious consumption of fluids, especially hot fluids—moderation in exercise, avoiding sea bathing, close rooms, warm clothing, and so forth. Soap should not be used in the bath. The sleeping-mattress and pillow should be covered with a finely woven grass mat, and the bed provided with what is known in the East as a "Dutch-wife"—that is, a hollow cylinder, 4 ft. by 8 or 10 in., of open rattan work, over which the arms and legs can be thrown, and unnecessary apposition of sweating surfaces so avoided. A punkah at night is a great comfort. Many things have been recommended as preventives; for example, rubbing the body over after the bath with the juice of a lemon, Jeyes' fluid or bran in the bath, etc. Every bath-room in the tropics should be provided with some mildly astringent and antiseptic dusting powder. A very good one consists of equal parts of boric acid, oxide of zinc, and starch. This should be freely applied, after careful drying of the skin, particularly to the axillæ, crutch, under the mammæ in women, and between the folds of skin in fat children and adults. A simple precaution of this sort saves much suffering both from prickly heat and epiphytic skin disease.

Durham recommends painting the patches with weak iodine or, better, rubbing in a solution of corrosive sublimate, 1 : 500–1 : 1,000. This he found very efficacious, curing the disease with certainty after one or two applications. He suggests the use of some form of obstetric soap as being less liable to lead, through inadvertence, to accidental poisoning.

The frequent application of a salicylic acid (1 dr.) and spirit (8 oz.) lotion has been advised. Pearse strongly recommends

Digitized by Google

the inunction of a mixture of almond oil and lanolin in the proportion of 8 to 1, and scented according to fancy. Gray considers thin flannel a better wear than cotton or linen as a preventive of prickly heat. Sometimes the following powder, gently rubbed in for five or ten minutes with a damp sponge, will cure bad patches of prickly heat: Sublimed sulphur, 80 parts; magnesia, 15 parts; oxide of zinc, 5 parts. Lotions of calamine, with or without hydrocyanic acid, or of carbolic acid, relieve the itching temporarily.

Fig. 205.—Leucodermia in a Sinhalese. (*Orig.*)

LEUCODERMIA (Fig. 205)

Synonym.—Vitiligo.

Leucodermia is extremely common throughout the tropics, and is by no means confined to any particular race. Almost any part of the body may be affected. The atrophied, unpigmented patches of skin slowly enlarge in a peripheral direction and may coalesce. Occasionally the whole body is affected and a certain amount of symmetry may be observed; the hair of the affected parts may also become white. The texture and glands of the skin remain normal. The etiology of the disease is unknown, but it is thought to be a trophoneurosis. No treatment is of any avail.

Digitized by Google

II.—BACTERIAL SKIN DISEASES

Tropical Sloughing Phagedæna

Synonym.—Ulcus Tropicum.

Definition.—A rapidly spreading but, as a rule, after a time, spontaneously arrested gangrene of the skin and subjacent tissues, resulting in the formation of a large sloughing sore. Though occasionally fatal, these sores almost always, under favourable conditions, granulate and cicatrize, or become chronic ulcers.

Geographical distribution.—Sloughing phagedæna is common in most tropical countries, particularly in those with a hot, damp climate. These sores are often named after those districts in which they are specially prevalent; thus we hear of Mozambique ulcer, Yemen ulcer, etc. They are found principally in jungle lands, less frequently in towns and well-settled districts. Whether tropical sloughing phagedæna and hospital gangrene—at one time so prevalent in the hospitals of Europe—are the same disease, it is difficult to say. They agree in some respects; but in the marked tendency of the tropical sore to self-limitation; and possibly, as Scheube points out, in its relatively feeble infective power, there is some indication of a specific difference.

Occasionally this disease assumes epidemic proportions. Thus, Lloyd Patterson described one such epidemic which "swept like a plague up the whole of Assam," seriously interfering with the efficiency of the labour force on the tea plantations.

This form of phagedænic ulcer was, according to Balfour, very common among the carriers attached to the East African Force during the War, and accounted for a considerable amount of invaliding.

Various bacteria and spirochætes have been described as possible germ causes of this disease. Vincent remarked the frequent concurrence of spirochætes and fusiform bacilli especially near the edges of the sores, an observation confirmed by several others, including Todd and Wolbach on the Gambia, and the Editor in Egypt and Palestine. Prowazek attributes these ulcers to *Spironema schaudinni*.

Although sloughing phagedæna is evidently a germ disease, it is not readily communicated by ordinary inoculation either to man or to the lower animals. Apparently a concurrence of certain unknown conditions is essential. Lloyd Patterson, however, by bandaging a swab smeared with discharge from a typical sore (discharge containing large numbers of his bacillus) on to the

Digitized by Google

surface of an abrasion from which the scab had been removed, succeeded in producing a characteristic sore, in the discharge from which his bacillus was present in great profusion.

Etiology.—Doubtless depending on the proliferation in the affected tissues of some specific micro-organism not yet satisfactorily separated, the germ of sloughing phagedæna attacks the healthy as well as the debilitated, young or old, male or female. It finds its special opportunity in the bodies of men who, from overwork, underfeeding, exposure, malaria, dysentery, scorbutus, and the like, are physically depressed. Thus it is apt to attack the half-starved, malaria-stricken pioneers in jungle lands, overdriven slave gangs, and soldiers campaigning in the tropics. In such circumstances a slight wound, an abrasion, even an insect-bite, or an old chronic ulcer may serve as the starting-point for one of these terrible sores. Where yaws and sloughing phagedæna are coendemic, the sores of the former may become infected with the virus of the latter, and serious sloughing and cicatricial contractions result. The feet and legs, being most exposed to injury, are the most frequent locations for this form of ulceration; but the arms or any other part of the body may also be attacked.

Symptoms.—If the disease occur in previously sound skin the first indication is the formation of a larger or smaller bleb with sero-sanguinolent contents. The formation of this may be attended with some pain and constitutional irritation. When, in the course of a few hours, the bulla ruptures, an ash-grey, moist slough is exposed. The sloughing process rapidly extends in all directions until the skin and subcutaneous fascia over an area of an inch to many inches in diameter are converted into a yellowish, moist, horribly stinking slough. After a few days the centre of the slough begins to liquefy, the sore still continuing to extend at the periphery. In the course of a week or longer the sloughing process may cease and the slough be gradually thrown off. Then it is seen that not only have the skin and superficial fascia been destroyed, but that in bad cases possibly muscles, tendons, nerves, vessels, and even the periosteum of the bones, have shared in the gangrenous process. Fortunately in many instances the deeper structures are spared, the disease being relatively limited and superficial. Sometimes, however, important structures, including joints, bones, and large blood-vessels, are destroyed; in such cases, even if life be spared, great deformity may ensue from different forms of ankylosis, or from strangulation of a distal part by a contracting cicatrix.

When the disease attacks a pre-existing wound or sore, the

Digitized by Google

granulating surface of this becomes dry, and rapidly assumes the appearance and characters of a slough.

In sloughing phagedæna the neighbourhood of the sore is somewhat congested and swollen, particularly so if the patient has been obliged to use the limb. Constitutional disturbance may be considerable and of an adynamic type. On the other hand, it occasionally happens that large sores are attended with singularly slight local or general reaction. In bad cases a sapræmic condition is apt to supervene and carry off the patient; or death may occur from bleeding from the opening of a large blood-vessel.

Diagnosis has to be made from the ulceration of yaws, syphilis, oriental sore, varicose ulcers, and veld sore.

Treatment.—It is of the first importance to endeavour to correct any cachectic state which may be present. Thus good food, fresh vegetables, lime-juice, and quinine are almost invariably indicated. Opium in full doses, not merely to assuage pain, but on account of its special action on the phagedænic process, is usually of great service. Locally, an endeavour must be made effectually to destroy the germ by the application of some powerful and penetrating caustic to the diseased surface. With this view, on the strength of considerable experience, Manson recommended that the patient be put under chloroform and the slough thoroughly dissolved off by the free application of pure carbolic acid, a piece of lint on a stout stick being used as a mop for the purpose. Thereafter the limb should be elevated and placed under some improvised irrigator from which a weak, warm, antiseptic solution should continuously trickle over the now clean surface. If the phagedænic action recur the carbolic acid must be promptly reapplied as often as may be necessary. On healthy granulations springing up the ulcer is to be treated on ordinary principles. Patterson recommends a dressing of carbolic oil after the initial cauterization, and subsequently, when the sore is clean, a dressing of lead-foil such as is used for lining tea-chests.

Patients with this disease should be regarded as infective, and, so far as possible, isolated.

The most recent and successful treatment would appear to be with formalin. The strong commercial solution is applied lightly once a day for two or three days, followed by a bismuth-paste dressing directly a scab has formed. It may be necessary to repeat the treatment. Whenever available, X-rays should be tried. Sometimes recourse has to be had to amputation.

Digitized by Google

Veld Sore

Synonyms.—Septic Sore; Desert Sore; Barcoo Rot.

Definition.—A cutaneous ulceration of extreme intractability, affecting the exposed parts of the body, and accompanied by numbness of the skin, debility, and, it may be, signs of peripheral neuritis.

Geographical distribution.—This peculiar ulceration is widely distributed in the tropics and subtropics wherever desert conditions exist. It has long been known in Queensland and the Northern Territory of Australia. It affected the British troops in the Sudan and South African campaigns. In South Africa it is familiar to sportsmen and travellers. These sores caused a very considerable amount of disability in Gallipoli, Egypt, Palestine, and Mesopotamia during the War.

Etiology.—The cause of this condition has long been obscure. In 1916 Dr. Colin Craig, working in the Sinai Desert, demonstrated the diphtheria bacillus in the lesions. Whether this covers the etiology of all veld sores cannot at present be affirmed, but that a certain proportion are diphtherial in origin may be taken as established. By sterilizing the surface of the sore with absolute alcohol and scraping the clear surface, a pure culture of the Klebs-Löffler bacillus may be obtained on Löffler's serum. This organism is pathogenic to guinea-pigs and quails, and its lethal effects may be neutralized by injection of antidiphtheritic serum. In the serous contents of the blebs the typical granular bacillus may be observed in stained preparations.

The desert sores, as the Editor observed them among British troops, occurred most frequently in men of mounted units, especially those associated with camels. The rate of incidence coincided with a widespread epidemic of faucial diphtheria amongst the troops.

Symptoms.—The sores occur almost invariably on the exposed parts, mainly those covered by hairs, such as the dorsum of the hand, the forearm, elbow- and knee-joint. Sometimes the lesions occur on the face, over the eyebrows and on the cheeks. They may arise *de novo*, or be superimposed on some other abrasion.

A regular sequel of events precedes the actual ulceration. At first a *vesicle* full of straw-coloured fluid makes its appearance, generally in the vicinity of a hair-follicle; it may vary considerably in size. The pain it occasions is quite out of proportion to the size of the lesion. On bursting it leaves behind a shallow *ulcer* covered with a thin grey pellicle. The raw ulcerated surface is

Digitized by Google

exquisitely tender, and may continue to spread peripherally. (Fig. 206.)

After the inflammatory changes have lasted two or three weeks the ulcers enter upon a *chronic stage*. At this stage they are characteristic in appearance, and perhaps are more familiar to tropical practitioners and medical officers than when in the incipient stages.

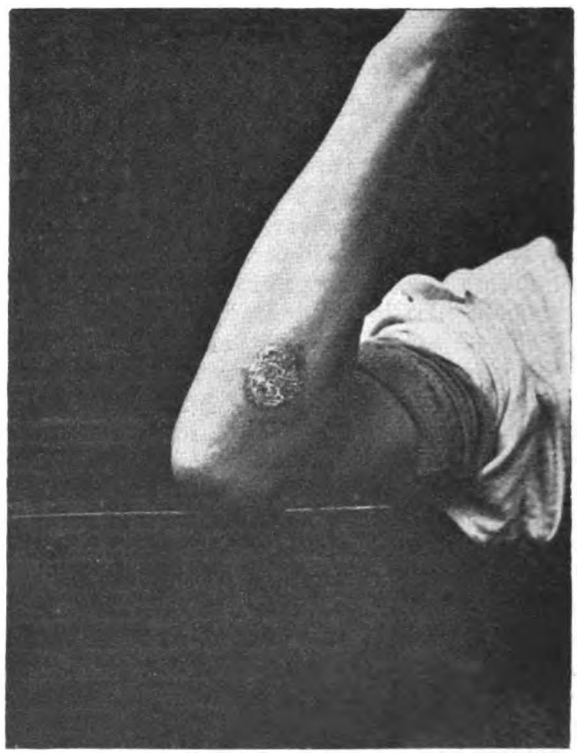


Fig. 206.—Veld sore.

Mesopotamian case of two and a half years' duration. Healed in ten days with ,000 units of antidiphtheritic serum.

The ulcers are punched-out, circular in outline, with undermined edges and thickened margins; their base is covered with grey-coloured and scaly débris, beneath which one can frequently distinguish an adherent membrane, but little or no pus is discharged. The peculiar ulceration which results is most intractable, and resists all external forms of medication; the edges become indurated, and the thickened tissue has a cyanotic appearance. In

Digitized by Google

sores in which healing does take place a thin paper-like scar remains, and persists for several years. The actual ulceration may continue for two years or longer.

The Klebs-Löffler bacillus can only be isolated with ease from the primary lesions; from the chronic ulcerations it is recovered with difficulty, being overgrown with staphylococci and other organisms of suppuration.

Typical diphtheritic pareses or paralyses have been observed in association with these sores. In one series this complication occurred in 27 per cent. of cases. Paralyses of the palate, arms, and legs have been observed. There may be ataxia, loss of knee-jerks, anæsthesia, and inco-ordination, recalling at first sight locomotor ataxia or beriberi; indeed, these diseases have been diagnosed in cases of this peripheral neuritis.

Treatment.—The specific treatment for this form of ulceration is antidiphtheritic serum, which has an almost miraculous effect in healing up ulcers that have persisted for a year or even more. At least 4,000 units should be given, and should be injected subcutaneously in the vicinity of the sores. The sores themselves may be dressed with lint soaked in the same serum or with weak formalin.

Prophylaxis.—Protecting exposed parts of the body, especially the knees, against abrasion, in desert regions where these sores occur, is obviously indicated. Mounted men should wear knee-breeches and should not be permitted to ride in shorts. The application of antiseptic lotions to any abraded surface at the earliest possible moment is also indicated. As there is some evidence that dried horse-manure may act as a nidus of the bacillus, care should be taken to avoid contact with this substance as far as possible.

Boils (Nile Boils)

The anatomical and clinical features of this painful affection are too familiar to require detailed description. Suffice it to say that a boil is produ ed by the proliferation of *Staphylococcus pyogenes aureus* and *albus*, *Streptococcus pyogenes*, or other pyogenic micro-organisms in the skin and subcutaneous tissue; that the organism gives rise to local and limited infiltration of the tissues with lymph which subsequently and rapidly dies, the necrotic core being surrounded by an areola of acute inflammation; that this core is separated by a process of sloughing and so got rid of, the resulting ulcer speedily healing and leaving a depressed scar which, when occurring about the legs, may become pigmented.

Digitized by Google

Though a self-limiting disease locally, it is nevertheless capable of being inoculated elsewhere in the same individual, both through a breach of surface and also by simple contact of the discharges with the skin, the micro-organism apparently entering by a hair-follicle. This auto-inoculability of boils is apt to be overlooked.

Conditions of debility, presumably by lowering resistance, predispose to boils; the subjects of diabetes are especially prone to them, the saccharine state of the blood or secretions seeming to be particularly favourable to growth of the specific germ.

Few Europeans in the tropics escape an attack of boils at one time or another. In some instances there is a succession of crops, the individual boils being so numerous that the patient is quite unfitted for work by the attendant pain and fever. In certain years so many members of a community are attacked that the disease may be described as being epidemic. These epidemics, occurring when some particular fruit is in season, are very generally, but probably incorrectly, attributed to the use of the fruit in question. Mangoes, it may be erroneously, are frequently held responsible.

Treatment.—Any constitutional irregularity must be treated appropriately. Malaria demands quinine; anæmia and debility, iron and wine; constipation, aperients; diabetes, a suitable diet. One has never seen any good from such vaunted specifics as calcium sulphuret, tar water, or yeast.

Boils ought never, unless in very exceptional circumstances, to be poulticed. Poulticing, although it may relieve the pain of the existing boil, is prone to be followed by more boils in the area sodden by the heat and moisture. Neither should boils be incised or squeezed. The only exception to the rule of not cutting is in the case of boils occurring in the scalp or in the axilla. In the former situation, unless opened early, they are apt, especially in young children, to burrow and cause troublesome abscesses; in the latter situation boils tend to be very indolent and painful, and do not readily spontaneously break through the lax integuments.

In any situation in which the boil is liable to be irritated by pressure or clothing, it is sometimes a good plan to cover the part with a circle of wash-leather spread with soap plaster, and having a small hole cut in its centre corresponding to the apex of the boil. When a boil opens, the discharge must be kept from soiling the adjoining skin, and the patient must be warned against touching the skin elsewhere with pus-soiled fingers. The parts must be frequently cleansed with 1 : 1,000 corrosive sublimate lotion,

Digitized by Google

powdered with boric acid, and covered with a dry, absorbent antiseptic dressing. A threatening boil may often be aborted by touching the little initial itching or vesiculated papule with some penetrating antiseptic, as iodine tincture, or by painting it with collodion. A very successful method is to drill slowly into the centre of the papule with a pointed pencil of hard wood dipped in pure carbolic acid. The point of the pencil should penetrate at least an eighth of an inch, and should be frequently recharged with the acid during the drilling process; the pain is trifling. In this way, in a severe attack of furunculosis, boil after boil may be aborted and the attack brought to an end. In obstinate chronic furunculosis excellent results have occasionally attended treatment conducted on Wright's method of exalting the opsonic index of the blood by injections of killed cultures of the patient's pyogenic micro-organisms. An autogenous vaccine ought to be used wherever possible, beginning with a dose of fifty millions and working up to three hundred millions of organisms.

In severe cases change of air may be necessary.

Pemphigus Contagiosus (Pyosis Mansoni)

Definition.—A non-febrile, highly contagious skin disease, peculiar to warm countries. It is characterized by the formation of large vesicles or bullæ which are unattended by marked inflammation, ulceration, or the formation of crusts or scars.

Geographical distribution.—Pemphigus contagiosus is very common in South China during the hot weather; in some years it may even be described as epidemic. It is perennial in the Straits Settlements, and it is known in Ceylon, Madras, in North Queensland, Japan, and America. Doubtless, although it has escaped notice by most medical writers, it is common enough elsewhere in the tropics, or wherever heat and moisture combine to bring about a state of skin favouring its development on the infective material being applied. It is especially common in schools and similar institutions where large numbers of children are thrown much together; they readily pass the disease one to the other. European children are more prone to it than native children; European adults are by no means exempt, but the native adult is rarely affected.

Symptoms.—Pemphigus contagiosus closely resembles certain forms of the impetigo contagiosa of temperate countries, and may be a variety of this class of skin disease. The individual lesions, as can readily be ascertained by inoculation experiments, begin as minute erythematous specks, which rapidly proceed to

Digitized by Google

the formation of vesicles, bullæ, or even large pemphigus-like blebs. The little blister springs abruptly from sound skin; there is no, or very little, areola of congestion. For a short time the hemispherical bleb is beautifully pellucid, tense, and shining. Presently the serous contents become somewhat turbid, and the blister gets flaccid and dull. At this stage, from scratching or from pressure, the blister is generally ruptured. The morbid process does not at once come to an end, but proceeds as an advancing, eccentrically spreading exfoliation of the epidermis—an exfoliation which may not cease to advance until an area an inch or more in diameter is denuded of epithelium. Then, in that particular spot, the disease stops, a pinkish, slightly glazed-looking patch, rarely covered with a tissue-paper-like scale, remaining for some time. Occasionally, after the rupture of the primary bleb, vesication may continue in the peripheral portion of its remains. Only one or two blebs may be visible on the entire surface of the body; generally there are many, the disease being spread by the fingers in scratching or rubbing.

Pemphigus contagiosus may occur in almost any part of the body. In young children it is usually diffuse; in adults it is mostly confined to the axillæ and crutch. In these situations it gives rise to much irritation and discomfort, owing to the successive crops of bullæ running into each other and rendering the parts raw and tender, and predisposed to boils or some form of eczematous intertrigo. During warm, moist weather it may be kept up indefinitely by auto-inoculation.

Etiology and pathology.—Like ordinary impetigo contagiosa, this is undoubtedly a germ disease. Manson found a diplococcus in the epidermis and fluid of the blister; whether this is the special bacterium responsible for the disease, cultivation and inoculation experiment have not yet decided. It is probable that one of the pyogenic cocci is responsible for this affection, which resembles in so many ways impetigo contagiosa.

Diagnosis.—Absence of constitutional symptoms, or a history of such, distinguishes pemphigus contagiosus from chickenpox. Absence of trichophyton elements and of a well-defined, slightly raised, festooned, and itching margin, together with the presence of large blebs and scaling of the epidermis, distinguishes it from ordinary forms of body ringworm—a disease with which, when occurring in the armpits and crutch in adults, it is frequently confounded.

Treatment.—Cleanliness, the frequent use of a bichloride of mercury lotion (1 : 1,000), and a dusting powder of equal parts

Digitized by Google

of boric acid, starch, and zinc oxide, are speedily effective. In the school and nursery those responsible for the care of children must be informed of the contagiousness of this unpleasant affection, and measures be instituted accordingly.

III.—FUNGOUS DISEASES

Mycetoma

Synonyms.—Madura Foot; Pseudactinomycosis.

Definition.—A fungous disease of warm climates, affecting principally the foot, occasionally the hand, rarely the internal organs or other parts of the body. It is characterized by enlargement and deformity of the part; an oily degeneration and general fusion of the affected tissues; the formation of cyst-like cavities communicating by sinuses, and containing mycotic aggregations in an oily purulent fluid which escapes from fistulous openings on the surface. The disease runs a slow course, is never recovered from spontaneously, and, unless removed, terminates after many years in death from exhaustion.

History and geographical distribution.—The disease has been known since 1712, when it was first described by Kämpfer. Subsequently it was confused with tuberculous disease, but Carter, from 1865 to 1874, furnished the information upon which modern descriptions of the disease are based. Much further information has since been supplied by Bouffard and Brumpt.

In India mycetoma is endemic in widely scattered districts, in some instances whole provinces, as that of Lower Bengal, enjoying an almost complete immunity. It appears to be acquired only in rural districts, the inhabitants of the towns being exempt. Among the more afflicted districts may be mentioned Madura —hence the name "Madura foot" by which mycetoma is often known—Delhi, various places in the Punjab, Kashmir, and Rajputana. In recent years we have accounts of its occurrence with some degree of frequency in Senegambia, Somaliland, Algeria, Egypt, the Sudan, Madagascar, Cochin China, Italy, the United States, and South America. It is probable that, in time, forms of mycetoma will be found to be endemic in many warm countries in which they have hitherto escaped recognition.

Symptoms.—Mycetoma begins usually, though by no means invariably, on the sole of the foot. The first indication of disease is the slow formation of a small, firm, rounded, somewhat hemispherical, slightly discoloured, painless swelling, perhaps about ½ in. in diameter (Fig. 207). After a month or more this swelling

Digitized by Google

may soften and rupture, discharging a peculiar viscid, syrupy-looking, oily, slightly purulent, sometimes blood-streaked fluid containing in suspension certain minute, rounded, greyish or yellowish particles

Fig. 207.—Mycetoma of about two years' standing. (*After Legrain.*)

often compared to grains of fish-roe. In other examples of the disease the particles in the discharge are black, having the size and appearance of grains of coarse gunpowder. Sometimes these

Digitized by Google

particles are aggregated into larger masses up to the size of a pea. In time additional swellings, some of which break down and form similar sinuses, appear in the neighbourhood of the first, or elsewhere about the foot. For the most part the sinuses are permanent, healing up in a very few instances only. Gradually the bulk of the foot increases to perhaps two or three times the normal volume (Fig. 208). There is comparatively little lengthening of the foot; but there is a general increase in thickness, so that in time the mass comes to assume an ovoid form, the sole of the member becoming convex, the sides rounded, and the anatomical points obliterated. The toes may be forced apart, bent upwards at the tarso-phalangeal joints, or otherwise misdirected; so that on the

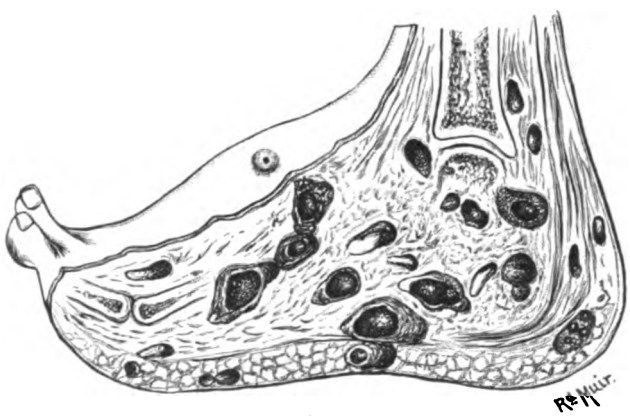


Fig. 208.—Section of a Madura foot. (*T. R. Lewis.*)

foot being placed on the ground the toes do not touch it. The surface of the skin is roughened by a number of larger or smaller, firmer or softer hemispherical elevations, in some of which the orifices of the numerous sinuses open. Most of these orifices are easily made out; others are not so apparent, their position being indicated, and at the same time concealed, by a bunch of pale, flabby, fungating, and but slightly vascular granulations. In the latter the orifice may be hard to find. Once the probe is inserted, the instrument readily passes to a considerable depth, even to the bone; in advanced cases it can be carried through the softened tissues with the greatest ease in almost any direction, and without causing much pain or hæmorrhage.

The discharge issuing from the sinuses differs in amount in different cases, and from time to time in the same case; whether

Digitized by Google

profuse or scanty, it always exhibits the same oily, mucoid, slightly purulent appearance, and may stink abominably. With a very few exceptions it contains either the grey or the black grains already referred to; rarely, similar bodies of a reddish or pink colour.

To the touch the swollen foot feels somewhat elastic and does not readily pit on pressure. The sensibility of the skin is preserved. Although complained of in some instances, severe pain is rarely a prominent feature. The principal complaint is of inconvenience from the bulk and weight of the mass, and, in advanced cases, of the uselessness of the limb for locomotion. In time the foot is no longer put to the ground, different unnatural styles of progression being adopted by different patients.

As the foot enlarges the leg atrophies from disuse; so that in the advanced disease an enormously enlarged and misshapen foot, flexed or extended, is attached to an attenuated leg consisting of little more than skin and bone. In some cases the tibia or, if the hand is the seat of invasion, the bones of the forearm are involved; in others the disease at first may be confined to a toe, or a finger, or other limited area. In a very few instances the seat of the disease is the knee, thigh, jaw, or neck. Unless the case be one of actinomycosis the internal organs are never specifically implicated, either primarily or secondarily. The lymphatic glands, likewise, although they may be the subjects of adenitis from secondary septic infection, are very rarely involved.

After ten or twenty years the patient dies, worn out by the continued drain, or carried off more suddenly by diarrhœa or other intercurrent disease.

Classification, etiology, and histology.—The tropical forms of mycetoma were formerly classified according to the colour of the mycotic particles in the discharge. Thus we had the white or ochroid, the black or melanoid, and the red forms of mycetoma, the last being a very rare variety. Brumpt's investigations have made possible a classification more scientific than this crude clinical one; the latter, therefore, has to be abandoned.

This authority distinguishes eight different kinds of mycetoma, two of which are caused by species of *Discomyces*. Of the other six, two are certainly caused by species of *Aspergillus*. The remaining four are also probably due to species of aspergillus, but, in the absence of cultural evidence, he places them in two provisional groups: one of these, embracing the unpigmented species, he names *Indiella;* the other, the pigmented species, he calls *Madurella*. Moreover, he has shown that the fungi which

Digitized by Google

give rise to mycetoma may present not only resisting forms such as sclerotia and chlamydospores, but also characteristic spore apparatus (*Aspergillus nidulans*, *A. bouffardi*). The species are as follows :—

i. Actinomycotic Mycetoma

Caused by the ray-fungus, *Discomyces bovis* (Harz, 1877). Actinomycosis has a worldwide distribution and is a common disease of cattle. It occurs also in hogs. In men it may attack the extremities, giving rise to a tumour clinically indistinguishable from other kinds of mycetoma, or it may develop in the jaw, the tongue, lungs, liver, brain; and occasionally the primary lesion may be followed by metastases in all parts of the body.

The fungus of actinomycosis develops equally well in most tissues. It destroys bone by erosion and spares only nerves and tendons. The pus from the affected region contains small yellowish granules ("sulphur grains") of irregular shape, attaining at most 0·75 mm. in diameter. They are soft and consist of an inextricable felted mass of mycelia. The threads are radially arranged at the periphery of the grain, and their free extremity widens into a bulbous, club-like termination (10–20 μ long by 8–10 μ wide). These clubbed ends have been looked upon by several authors as forms of degeneration. Brumpt points out that they consist of young, active protoplasm, and holds that they are functionally hypertrophied while elaborating food for the colony. In old grains the clubs disappear, their protoplasm being utilized in the formation of spores.

This fungus gives rise to ramified sinuses which extend in all directions, opening at the surface by numerous vents. The sinuses are surrounded by a thick fibrous sheath of connective tissue. The centre of the largest tunnels is softened, the youngest grains being at the periphery surrounded by polynuclear cells and almost in contact with the sclerosed tissues which separate the cavities and sinuses.

The parasite has been successfully cultivated, and the disease has been inoculated both with the natural and the artificially grown organisms.

Discomyces bovis lives saprophytically on certain plants. It has been found on the spikelets of cereals (*Hordeum murmium* L., *Phleum pratense* L., etc.), and is therefore probably inoculated through the skin or mucous membranes in the same way as the fungi which give rise to other kinds of mycetoma.

The diagnosis of the disease from tertiary syphilis and bone tuberculosis rests on the characteristic grains present in the pus.

The disease is progressive and of grave import. The treatment is largely surgical. In early cases iodide of potassium in doses of from 40 to 60 grains daily has proved advantageous, and in some cases even curative.

ii. Vincent's White Mycetoma

Caused by *Discomyces maduræ* (Vincent, 1894). This kind of mycetoma is common and widely distributed. It has been observed in Algeria, in Abyssinia, in Somaliland, in Cyprus, in India, in the Argentine, and in Cuba.

It runs a slow course. Unlike *D. bovis* and other mycetoma-producing fungi, it does not destroy bone, and does not seem to act directly on the general health of the patient, though ultimately and indirectly it may bring about cachexia.

The grains formed by *Discomyces maduræ* vary in size from that of a pin's head to that of a pea. They are of a yellowish-white colour, present

Digitized by Google

a mulberry-like surface, are soft and easily crushed. Their mode of growth is absolutely characteristic. The grain throws out from its periphery radiating filaments. Between these fungus threads are numerous lymphocytes (likewise arranged in radial series) embedded in an amorphous substance, probably arising from the destruction of lymphocytes, epithelial cells, and macrophages on which the mycelium feeds. The crown of amorphous rays round the grain is typical. The grain is surrounded by numerous polynuclear leucocytes. Having attained from 1 to 1·5 mm. diameter, the grain projects small shoots which become detached from the parent grain, enlarge, and reproduce the characteristic radial structure. Other grains form also, and, after a time, the typical large mulberry granule is formed, the central grains degenerating. The grains are found in cavities surrounded by inflammatory connective tissue permeated by polynuclear cells and occasionally giant cells.

iii. Nicolle's White Mycetoma

Caused by *Sterigmatocystis* (*Aspergillus*) *nidulans* (Eidam, 1883). So far only one case has been observed—in Tunis—but probably it occurs in many places, the parasite *S. nidulans* being widely distributed. The grains formed by this fungus may also attain the size of a pea, but they differ from those of *Discomyces maduræ*, inasmuch as they are more or less spherical and present a smooth surface.

In this form of mycetoma the bones are attacked and destroyed.

iv. Bouffard's Black Mycetoma

Caused by *Aspergillus bouffardi* (Brumpt, 1906). This form was discovered by Bouffard at Djibouti, Somaliland. The grains are quite characteristic. They are black in colour and vary in size from a pin's head to that of No. 1 shot. They present a mulberry-like surface which is smooth and glossy. They are somewhat elastic, but break when pressed. Their structure is remarkable; it consists of a coiled-up mass. Maceration in water for about twenty-four hours causes the grain to unfold. Sections show that the grain is composed of a densely felted mycelium of a silvery-white colour, with a peripheral zone of irregularly moniliform threads with terminal chlamydospores cemented together by a dark brown interstitial substance.

The grains are found in the cellular tissue, always singly and within small cavities. Each grain is surrounded by enormous giant cells and by epithelioid cells of all sizes, and is enclosed in a characteristic shell of connective tissue.

This kind of mycetoma appears to be more amenable to treatment. Bouffard's and Bovo's cases were radically cured by curettage. In Bovo's case a secondary extension to the groin lymphatics of the affected side had suggested the diagnosis of melano-sarcoma.

v. Carter's Black Mycetoma

Caused by *Madurella mycetomi* (Laveran, 1902). This mycetoma has a very wide distribution. It has been observed in Italy, in Africa (Senegal, French Sudan), and in India.

The grain formed by *Madurella mycetomi* is dark brown or black in colour. It measures 1 to 2 mm. in diameter, is hard and brittle; its surface is irregular and frequently presents pointed eminences which differentiate it from the larger and smooth grains of *Aspergillus bouffardi*. The grain is composed of

Digitized by Google

white threads, always over 1 μ in diameter and attaining at times 8 to 10 μ, which secrete a dark-brown substance that cements them together. The grain is first surrounded by giant cells, epithelioid cells, and numerous polynuclear cells, and shows numerous chlamydospores at the periphery. Then a thick capsule of fibrous connective tissue forms round it. This puts an end to the vegetation of the fungus, which passes into a resting stage and is converted into sclerotia, in which form it is eliminated. This was shown by Carter as early as 1860. The grains form rapidly within the tissues. Brumpt reports a case in which they were eliminated in large numbers one month after the commencement of the disease.

Each grain may become the centre of an active colony, which continues to extend, destroying the surrounding tissues, until arrested by a barrier of sclerosed tissue. Thus large tumours may be formed. In very old grains the mycelium presents cavities filled with numerous chlamydospores. Sometimes, on account of unfavourable conditions, certain lobes of the fungus separate from the rest of the colony and become independent grains. This mode of vegetation, characteristic of the species, gives to the lesions a typical rosette-like appearance.

In a second species, *M. tozeuri* (Nicolle and Pinoy, 1908), described in South Tunisia, the mycelial elements follow the course of the smaller blood-capillaries.

vi. Brumpt's White Mycetoma

Caused by *Indiella mansoni* (Brumpt, 1906). This form was described from a specimen of Indian origin in the museum of the London School of Tropical Medicine.

The grains peculiar to this form are hard, white, and very small, varying in size between $\frac{1}{3}$ and $\frac{1}{4}$ mm., and having a lenticular shape. Some are bean-shaped and flat. To study their structure it is necessary to boil them first in a solution of caustic potash. The hyphal threads are large and closely set, but without any cementing substance between them. The periphery of the grain contains numerous large chlamydospores with thick wall and full of protoplasm.

The grains of *Indiella mansoni* are always numerous within the inflammatory tissue. The latter is brownish and is not surrounded by a well-marked sheath of connective tissue as in other mycetomas. It contains numerous polynuclear cells, a few lymphocytes, and some macrophages.

vii. Reynier's White Mycetoma

Caused by *Indiella reynieri* (Brumpt, 1906). This form was found in Paris by Reynier.

The grains may attain 1 mm. in diameter; they are soft, white, and consist of a coiled-up strand which gives them a peculiar appearance resembling the excrement of earthworms. They are made up of a dense felting of hyphal threads, the peripheral branches of which usually terminate in chlamydospores divided into two or three compartments. The hyphæ are bound by a scanty cement, which is easily dissolved out by boiling in caustic potash.

viii. Bouffard's White Mycetoma

Caused by *Indiella somaliensis* (Brumpt, 1906). This form is perhaps even more common in India than Vincent's white mycetoma. Bouffard has found it twice in Somaliland.

Digitized by Google

Indiella somaliensis is a most destructive fungus. In a foot examined by Brumpt all the muscles, tendons, and bones had been replaced by sclerosed tissues more or less homogeneous and presenting numerous sinuses full of yellowish grains clustered together like fish-roe, and many small inflammatory nodules containing one or more grains.

The grains vary in colour from white to reddish yellow; they are small, smooth, and attain on an average about 1 mm. in diameter. They are spherical when single, but polyhedral from reciprocal pressure when clustered in masses. The parasite in its earliest stage is always found in a giant cell, showing as an irregular mass which stains more deeply than the enclosing cell. Usually several infected cells coalesce; the grain which results is surrounded by an amorphous layer produced by the destruction of the elements which form its substratum. The grains are not enclosed within nodules, as is the rule in certain mycetomas, but spread exactly like those of actinomycosis.

In the amorphous zone of cellular detritus Brumpt found a discomyces which seems to live symbiotically with *Indiella somaliensis*. In attempts at culture Bouffard found that this discomyces was the only organism that grew. Other investigators—Boyce, Vincent, Musgrave and Clegg, etc.—have cultivated a streptothrix from the white variety, differing from the actinomyces in producing no pigment and forming white raised colonies on agar. Probably there are several conditions in actinomycosis, as in mycetoma, bearing a general resemblance to each other, but differing slightly according as they are produced by different species of streptothrix.

Morbid anatomy.—On cutting into a mycetomatous foot or hand the knife passes readily through the mass, exposing a section with an oily, greasy surface, in which the anatomical elements in many places are unrecognizable, being, as it were, fused together, forming a pale, greyish-yellow mass. The bones in parts have entirely disappeared; where their remains can still be made out the cancellated structure is very friable, thinned, opened out, and infiltrated with oleaginous material. Of all the structures the tendons and fasciæ seem to be the most resistant.

The most remarkable feature revealed by section is a network of sinuses and communicating cyst-like cavities of various dimensions, from a mere speck to a cavity an inch or more in diameter. Sinuses and cysts are occupied by a material unlike anything else in human morbid anatomy. In the black varieties of mycetoma this material consists of a black or dark brown, firm, friable substance which, in many places, stuffs the sinuses and cysts; manifestly it is from this that the black particles in the discharge are derived. In the white varieties the sinuses and cysts are also more or less stuffed with a white or yellowish roe-like substance, evidently an aggregation of particles identical with those escaping in the corresponding discharge. The black substance, which can be readily turned out, is moulded into truffle-like masses,

Digitized by Google

ranging in size from a mere grain to a small apple, according to the capacity of the cysts or sinuses containing it. The roe-like particles in the white varieties are held together by a softer, cheesy-looking material. The sinuses and cysts occupy the bones, muscles, or fasciæ indiscriminately; they are found principally in the fat and the connective tissue. They are lined with a smooth membrane, adherent when in the soft tissues, but capable of being enucleated when in the bones. Some of the cysts do not communicate with sinuses; most of them, however, do so, and with each other, opening on the surface of the skin at the mamillated fistulæ already referred to. In the very rare red variety the colour of the accretions is red or pink.

Under the microscope the mycotic elements can be readily recognized in the concretions. In microscopic sections of the tissues evidences of extensive degenerative changes, the result of a chronic inflammatory process, can be made out. An important feature as bearing on the pathology of the disease, and one which was long ago described by Lewis and Cunningham, has been insisted on more recently by Cunningham, namely, a sort of arteritis obliterans or extensive proliferation of the endothelium of the arteries, and, according to Vincent, a thickening of the adventitia of the vessels as well as of the capillaries in the more affected areas.

Mode of entrance of the fungus.—Little is known on this point. It is conjectured that the fungi live as parasites on certain plants, and that they may penetrate the tissues of man through a wound in the skin. The peculiar endemicity and geographical distribution of the disease, and the facts of its occurring almost invariably on the feet or hands, and principally in bare-footed agriculturists, favour this view.

Treatment.—The only effective treatment, in the case of implication of a considerable part of the foot or hand, is amputation. This must be performed well above the seat of the disease; for it must be borne in mind that the long bones may be implicated as well as the small bones, and that unless the entire disease be removed it will recur in the stump. Complete removal is not followed by relapse. If a toe, or a small portion of the foot or hand, is alone involved, this may be excised with success. Potassium iodide has been found to be beneficial in certain forms.

Blastomycosis

This term is used to indicate lesions, other than mycetoma, produced by the proliferation of certain yeast-like fungi in the

Digitized by Google

tissues. Normally these fungi are either saprophytic or live as parasites on animals or plants. They appear to be especially abundant in tropical countries. Doubtless they get access to the tissues through some wound or breach of surface. A number of species, distinguishable perhaps by the mycologists, have been described; for the clinician it suffices to know that in the morbid discharges and tissues they occur and are recognizable as yeast-like cells. In some instances the parasites are limited to one particular spot; in others they are more diffused, and may attack almost any organ or tissue. The following clinical types have been recognized:—

1. *Cutaneous.*—Patches of various dimensions of small warty excrescences with minute abscesses or encrusted ulcers, especially at the periphery of the patch.

2. *Oral.*—Lesions resembling the foregoing, which develop in or spread to the mucosa of the mouth and throat, and eventuate in deep ulceration and perhaps fatal destruction of the part. A form occurs on the tongue, leading to hypertrophy of the filiform papillæ, and causing a condition known as *lingua nigra.* The organism is known as the *Cryptococcus linguæpilosæ;* it has a double contour, is composed of oval yeast-like cells and mycelial elements, and can be cultivated on maltose-agar. Black tongue has been noted in Europe, and the Editor has seen a similar case in Ceylon.

3. *Coccidial.*—The skin lesions are similar to type 1, but usually larger and coarser. The viscera becoming involved, death ensues. In the affected tissues peculiar round bodies, 3 to 80 μ in diameter, many of them containing a multitude of spores, are a feature.

4. *Gluteal.*—There is extensive brawny thickening of one or both gluteal regions, the superjacent skin being thickened and coarse and perforated with the openings of many communicating sinuses. The condition is apt to be regarded as an aggravated form of fistula in ano.

5. *Pulmonary.*—A parasite, the *Cryptococcus capsulatus*, allied to *C. farciminosus* of the horse, has been demonstrated in the epithelial cells of the lung by Darling. The disease it produces resembles in many respects kala-azar, and is accompanied by splenomegaly, anæmia, irregular pyrexia, and leucopenia. Three cases have been described in Panama.

6. *Sporotrichosis.*—Gumma-like swellings in limbs or trunk, which enlarge and ultimately break down, leaving deep ulcers. The condition is due to an organism, *Sporotrichum beurmanni*, which usually exists saprophytically, and gains entrance to the

Digitized by Google

body through an abrasion of the skin or œsophagus. Occasionally the organism may be demonstrated in the blood, as recorded by Widal and Weill. The lymphatics, oral cavity, periosteum, muscles, or viscera may become involved. In the discharges and tissues the parasites are scanty, so that the mycotic nature of the disease can be made out only from cultures in maltose-agar tubes.

Pathological anatomy.—At the borders of the ulcerated tissue there are accumulations of inflammatory cells and other elements, especially giant cells, which include the organisms.

Diagnosis.—Usually these lesions in the first instance suggest syphilis or tuberculosis. Specific treatment and absence of reaction to tuberculin and of the bacillus of tubercle should lead to a careful search for yeast-like organisms in the discharges or scrapings. Widal and Abrami have found that the serum of sporotrichosis will agglutinate cultures of the specific organism; while Malvoy and Ricketts have demonstrated a complement-deviation test in blastomycosis, using old cultures of blastomyces as an antigen.

Treatment.—All forms of blastomycosis are exceedingly chronic and resistant to treatment. Surgical measures are useless, but large doses of the iodide of potassium or of sodium (20–30 gr. three times a day, well diluted) are sometimes effective, and should always be tried, and continued, if found beneficial, until cure is well established. The X-rays are at times a useful adjunct.

Dhobie's Itch (Tinea Cruris)

Etiology and nomenclature.—In view of the researches of Sabouraud and others on the ringworms of Europe, there can be little doubt that the ringworms of warm countries are attributable to a great variety of fungus forms, many of them probably derived from the lower animals. Although, in a general way, we are familiar with the clinical features of these ringworms, their specific germs have not as yet been very closely studied. By the lay public all epiphytic skin diseases—more especially all forms of intertrigo—are spoken of as dhobie's (washerman's) itch, in the belief, probably not very well founded, that they are contracted from clothes which have been contaminated by the washerman. There are many sources of ringworm infection in warm climates besides the much-maligned dhobie.

In the tropics, native children often exhibit dry, scurfy patches of ringworm on the scalp; and the skin of the trunk and limbs of adults is not infrequently affected with red, slightly raised,

Digitized by Google

itching rings, or segments of rings, of trichophyton infection. Sometimes these rings enclose areas many inches in diameter.

Pityriasis versicolor is also very common in the tropics. It is the usual cause of the pale, fawn-coloured, slightly scurfy patches so frequently a feature of the dark-skinned bodies of natives. On the dark-pigmented skins of negroes, Indians, and dark-complexioned Chinese the patch of pityriasis—contrary to what obtains in Europeans and light-skinned Chinese—is usually paler than the healthy integument surrounding it. The pigment in the fungus and the profuse growth of the latter conceal, as a coat of paint might, the dark underlying natural pigment of the skin, which, moreover, in certain cases seems to be affected (either increased or decreased) by the action of the fungus. The disease is nearly always seen in young adults, is favoured by excessive perspiration, and especially by flannel underwear, and is rarely seen in the aged. There are possibly several varieties of fungi involved in the production of pityriasis; besides *Microsporon furfur* the best-known is *Microsporon mansoni*, of which a culture in maltose-agar produces black hemispherical colonies, and correspondingly black patches on the affected skin.

The expression *dhobie's itch*, although applied to any itching, ringworm-like affection of any part of the skin, most commonly refers to some form of epiphytic disease of the crutch or axilla. There are at least three species of vegetable or bacterial parasites which in the tropics are prone to attack these situations—namely, the trichophytons or ordinary body ringworms, the *Microsporon minutissimum* of erythrasma, and the germ of the disease Manson described under the name pemphigus contagiosus.

Symptoms.—The suffering to which certain forms of dhobie's itch give rise is often severe. In hot damp weather especially the germs proliferate actively, producing, it may be, smart dermatitis. The excessive irritation thus set up leads to scratching and, very likely, from secondary bacterial invasion, to boils or small abscesses. The crutch, or axillæ, or both, are sometimes rendered so raw and tender that the patient may be unable to walk or even to dress. In some cases the clefts between the toes are attacked, giving rise to great itching. The irritations thus produced are usually worse at night, and may keep the patient awake for hours. Even in the absence of treatment, when the cold season comes round the dermatitis and irritation subside spontaneously. The affected parts then become dry, pigmented, and scurfy, and the fungus remains quiescent until the return of the next hot weather.

Diagnosis.—The diagnosis of mycotic dermatitis is usually

Digitized by Google

easily made. The festooned margin is almost conclusive. In the case of pemphigus contagiosus the characteristic blebs, the smooth, raw, or glazed surfaces, and undermined epidermic ring are usually very apparent and render diagnosis easy. When doubt exists, recourse to the microscope may be necessary; but, owing to the inflamed condition of the parts, there may be much difficulty in finding fungus elements even when the case is certainly epiphytic. A negative result is, therefore, not always conclusive against ringworm.

Manson is convinced that many cases of dhobie's itch are produced by *Microsporon minutissimum*, and that they are really inflamed erythrasma and not trichophyton ringworm. During cold weather one often sees, on the site of what, during the summer, had been a troublesome dhobie's itch, a brownish furfuraceous discoloration of the crutch or axilla. The same appearance has been remarked in Europe in Europeans who had suffered from dhobie's itch in the East, and on examining scrapings from the parts *M. minutissimum* has been found in abundance. It would seem, therefore, that during the heat and moisture of a tropical summer this generally very unirritating parasite becomes more active and excites dermatitis. The same may sometimes be seen in pityriasis versicolor. Experience shows that these cases of *Microsporon furfur* and *minutissimum* dhobie itch are more easily cured than the trichophyton varieties.

Treatment.—After a thorough use of soap and water, the application of Vleminck's solution of sulphide of calcium (1 oz. quicklime, 2 oz. precipitated sulphur, 15 oz. water, boiled together in an earthenware vessel till reduced to 10 oz.; decant the clear sherry-coloured fluid after subsidence) every night for three or four times generally brings about a rapid cure. If the parts are inflamed and tender the solution should be diluted to half or one-quarter strength for the first two applications. A preliminary soothing treatment by lead lotion, or an ichthyol or hazeline ointment, is desirable in such cases. A tincture of the leaves of *Cassia alata* painted on, or vigorous rubbing with the crushed leaves themselves, is equally successful. If these fail, chrysophanic acid ointment, 20 gr. to the ounce of vaseline, rubbed in twice a day till a slight erythema shows at the edge of the diseased patch, is almost invariably successful. When prescribing chrysophanic acid the physician must be careful to inform the patient of its staining effect on clothes; to warn him to stop its use so soon as the erythematous ring shows; and to be careful not to apply the ointment to the face. Glacial acetic acid, it is affirmed, cures

Digitized by Google

after one or two applications; the smarting its use entails is relieved by laying a lump of ice in a handkerchief on the part. An ointment of resorcin 1 dr., salicylic acid 10 gr., lanolin and vaseline 4 dr. each, to be applied twice a day, has been recommended. For the ringworms of the thick-skinned natives, linimentum iodi freely applied, and of double strength, is the best, the speediest, and most efficient remedy.

Prophylaxis.—The various forms of crutch dhobie's itch may be avoided by wearing next the skin short cotton bathing-drawers and changing them daily; at the same time powdering, after the daily bath, the axillæ and crutch with equal parts of boric acid, oxide of zinc, and starch.

Tinea Imbricata (Plate XXVI.)

Definition.—A form of body ringworm, until lately peculiar to certain Eastern oceanic tropical climates, produced by a trichophyton, and characterized by a concentric arrangement of closely set rings of scaling epidermis.

Geographical distribution.—This peculiar form of epiphytic disease is strictly confined to warm climates. It is principally met with in the Eastern Archipelago and in the islands of the South Pacific, although it has been found to extend westwards as far as Burma, and northwards as far as Foochow and Formosa on the coast of China. In many of the islands of the South Pacific it affects a large proportion of the inhabitants; in some islands quite one-half. There is good reason to believe that its area of distribution is gradually extending. We now hear of it in tropical Africa. Recently it has been described by Paranhos and Leme as occurring in the interior of Brazil. Once introduced, it spreads very rapidly in countries with a damp, equable climate and a temperature of 80° to 90° F. Very high or very low temperatures and a dry atmosphere are inimical to its extension.

Symptoms.—Tinea imbricata is easily recognized. At first it may be confined to one or two spots on the surface of the body; usually, in a short time, it comes to occupy a very large area. It does not generally affect the soles and palms, although it may do so; nor is the scalp a favourite site. Baker remarks that it avoids the crutch and the axillæ. With these exceptions it may, and commonly does, sweep over and keep its hold on nearly the entire surface of the body; so that after a year or two a large part of the body is covered with the dry, tissue-paper-like scales, arranged in more or less confused systems of concentric parallel lines, absolutely characteristic of the disease.

Digitized by Google

TINEA IMBRICATA.

PLATE XXVI.

Digitized by Google

Digitized by Google

An inoculation experiment readily explains the production of the scales, their concentric parallel arrangement, and the mode of extension of the patches. About ten days after the successful inoculation of a healthy skin with tinea imbricata, the epidermis at the seat of inoculation is seen to be very slightly raised and to have a brownish tinge. Presently the centre of this brownish patch—perhaps a quarter of an inch in diameter—gives way, and a ring of scaling epidermis, attached at the periphery, but free, ragged, and slightly elevated towards the centre of the spot, is formed. In a few days this ring of epidermis has extended so as to include a larger area. A second brown spot then appears at the site of the first brown spot and in the centre of the primary scaling, expanding ring. This second spot, in its turn, gives way, producing a second and similar scaling ring, which also expands, following the first ring in its extension. Later, a third and fourth ring form in the same way; and so on, until a large area of skin is covered with one or more systems of concentric parallel scaling rings, which follow each other over the surface of the body like the concentric ripples produced by a stone falling into a pool of water.

The scales, if not broken by rubbing, may attain considerable length and breadth; but, of course, their dimensions are in a measure determined by the amount of friction they are subjected to. Usually they are largest between the shoulders—that is, where the patient has a difficulty in scratching himself. The lines of scales are from $\frac{1}{3}$ to $\frac{1}{2}$ in. apart. The hair of the scalp is not injured.

The fungus.—On detaching a scale and placing it under the microscope, after moistening with liquor potassæ, a trichophyton-like fungus can be seen in enormous profusion. The parasite evidently lies between epidermis and rete, and by its abundance causes the former to peel up. As the fungus does not die out in the skin travelled over, it burrows under the young epithelium almost as soon as the latter is reproduced. Hence the peculiar concentric scaling and the persistency of the disease throughout the area involved. When the scales are washed off by the vigorous use of soft soap and hot water, the surface of the skin is seen to be covered with parallel lines of a brownish colour—evidently the slightly pigmented fungus proliferating and advancing under the young epidermis. Burgess and Castellani have succeeded in cultivating the true parasite, and by inoculation of cultures have reproduced the skin lesions. According to Castellani there are two species, *Endermophyton concentricum* and *E. indicum*. The

Digitized by Google

cultures are obtained by immersing the scales in alcohol for five to ten minutes and then placing them, one scale to each tube, in glucose broth. After five or ten days the scales, if uncontaminated, are transferred to solid media, and growth takes place in three or four weeks.

Diagnosis.—From ordinary ringworm tinea imbricata is easily distinguished by the absence of marked inflammation or congestion of the rings, by the abundance of the fungus, by the large size of the scales, by the concentric arrangement of the many rings or systems of rings, by the non-implication of the hair, and, according to Baker, by the avoidance of crutch and axillæ. From ichthyosis it is distinguished by the concentric arrangement of the scaling, by the peripheral attachment of the scales, and by the presence of abundant fungus elements.

Treatment.—The best treatment for tinea imbricata in natives is the free application of strong linimentum iodi. Limited patches might be treated with chrysophanic acid ointment (20 gr. to the ounce) or by rubbing with the bruised leaves of *Cassia alata*. Paranhos and Leme recommend a tepid alkaline bath of sodium bicarbonate (1 kilogramme to 20 litres of water), followed by the application of ocalia perdiceps 50 grm., glacial acetic acid 15 grm., macerated for two days in glycerinated water (10 per cent.) 985 grm., and then filtered. Sulphur ointment, or sulphur fumes, act very slowly and unsatisfactorily. Clothes should be boiled or burned.

Prophylaxis.—Daniels relates that tinea imbricata is a comparatively rare disease in Tonga. This circumstance the natives attribute to their custom of oiling the body. Since the Fijians adopted the same practice the disease has become somewhat less prevalent among them. Personal cleanliness, and the immediate and active treatment of any scaling spot, should be carefully practised in the endemic countries.

In Tahiti the use of chrysophanic acid is now general among the natives; as a consequence the disease is not so prevalent there as it was only a few years ago.

PINTA

Synonym.—Caraate.

Definition.—An epiphytic disease characterized by peculiar pigmented patches on the skin.

Geographical distribution.—In certain districts in tropical America, especially along the river banks, in Mexico, Central America, Venezuela, Colombia, Bolivia, and one or two places

Digitized by Google

in Peru, Chile, and Brazil—the district between the Juciparana and the Santo Antonio rivers—there occurs an epiphytic skin disease characterized by peculiar red, or blue, or black, or white piebald spotting of the skin of a part, or of the whole, of the body. The patient emits an offensive odour, sometimes compared to that of a mangy dog or of dirty linen. Desquamation and itching of the patches are also features of the disease. It entails no constitutional disturbance and no danger to life. As in other epiphytic diseases, want of personal cleanliness has a great deal to do with the prevalence of pinta in the districts mentioned, for it is rare in cleanly whites or well-to-do negroes; the dirty Indians and the poor half-castes are those most frequently affected. In some districts it occurs in nearly a tenth part of the inhabitants, in others nearly the entire population is affected. Possibly it is also present on the West Coast of Africa and in the Malay States.

Symptoms.—Pinta commences at one or two points, the rest of the surface of the skin becoming infected in turn by extension or by autocontagion. At first the hands, or face, or some other exposed parts, are attacked. The original patch may be white, red, blue, or black. It gradually increases in size, becoming scurfy and itchy, particularly when the surface is warm. As the patches spread they assume a variety of shapes. Fresh spots appear in the neighbourhood of the parent spots, into which, in course of time, they tend to merge; so that ultimately large patches of discoloured skin are formed. The palms of the hands and the soles of the feet are not attacked. On the scalp becoming affected the hair turns white and thin, and ultimately falls out. When fully developed the disease produces a very grotesque appearance. It is probable that the white patches in a proportion of cases are not epiphytic, as they neither itch nor desquamate; very likely they are ordinary leucodermia, possibly brought about through disturbance of the natural pigmentation by a parasite which had subsequently died out. Sensation and the glandular functions of the skin are not affected. In consequence of the scratching, the implicated parts may become cracked or ulcerated.

Two types of the disease have been named—the superficial epidermic and the deep epidermic: the former being represented by black and blue patches which spread rapidly; the latter including the red and white patches, apparently involving the rete and deeper layers of the epidermis, spreading more slowly, and, at the same time, being more difficult to cure. The various forms and colours may concur in the same individual; but a given patch, once established, does not change colour.

Digitized by Google

Pinta is contagious. It attacks both sexes and any age. Unless properly treated it may last for years.

Etiology.—If one of the scales is moistened with liquor potassæ

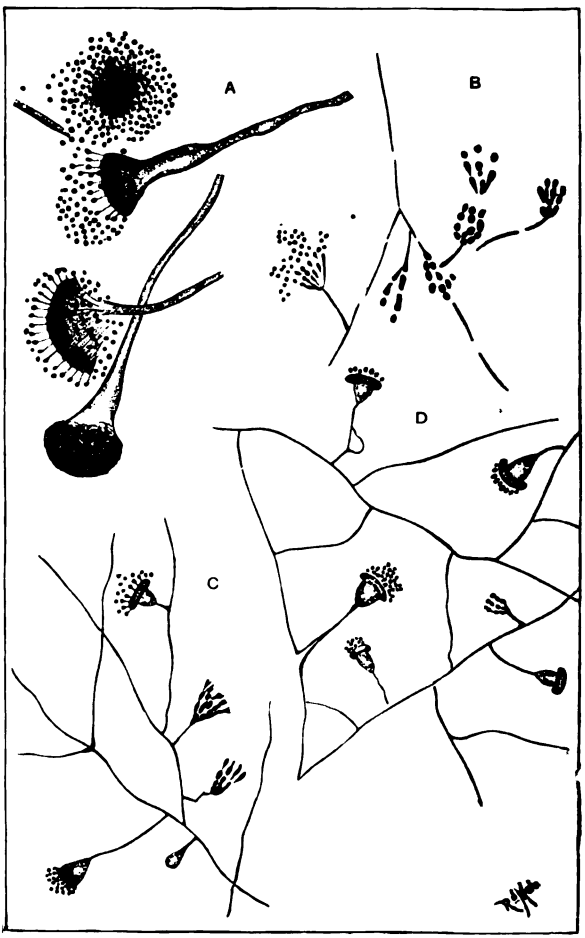


Fig. 209.—Fructification of cryptogamic epiphytes in pinta.
(After Montoya y Florez.)
A, Red pinta; B, dark violet pinta; C, grey-violet pinta; D, blue pinta.

and placed under the microscope, black spores and a white, highly refracting mycelium are found (Fig. 209). The spores are round or oval, measuring 8 μ to 12 μ in diameter. Abundant pigment

Digitized by Google

is seen floating in a yellowish fluid in the interior of the spore. The mycelial filaments are short, non-branching, tapering from a broad base to a blunt point by which each filament is attached to a single spore, like the stalk to a cherry. The mycelium measures from 18 μ to 20 μ in length by 2 μ in breadth. The differences in the colour of the patches probably depend on differences in the pigmentation, or kind, of the fungus. Such is Gastambide's description of the parasite—a description which, to some extent, is borne out by Osborne Browne.

It is said that violet pinta is caused by a mould, *Aspergillus pictor*, while the grey variety is due to *Penicillium montoyai*; a species of *Montoyella* is said to cause the red and black varieties.

Diagnosis.—This disease is readily diagnosed from leprosy by the absence of anæsthesia in the patches, and by the colour of the spots; from erythrasma, from ringworm, and from pityriasis versicolor, by the colour and by the microscopic characters of the fungus.

Treatment.—Chrysophanic acid, preparations of sulphur, strong liniment of iodine, and other epiphyticides are indicated. Cleanliness and the destruction of old clothes are indispensable.

Piedra

This peculiar disease of the hair is very common in certain districts of Colombia, South America. So far as is known, it is confined to the inhabitants of that country, of whom a considerable proportion, both male and female, and apparently belonging to all the races represented there, are affected.

The hairs of the affected scalp are dotted over at irregular intervals with numerous (twenty-three in a hair 60 cm. in length) minute, gritty nodosities. These, barely visible to the naked eye, are distinctly perceptible to the touch when the hair is drawn between finger and thumb. The affected hairs are bent and twisted, and tend to produce matting and knotting. The little nodosities, which, though very firm, are not so hard as the name piedra (a stone) would indicate, being easily cut through with a sharp knife or scissors, are paler than the hair which they surround, or partly surround, like a sheath. When a comb is drawn through the hair a sort of crepitation is produced, doubtless by the friction against the hard particles.

Etiology.—Under the microscope the excrescences are found to consist of a number of spore-like bodies, *Trichosporon giganteum*, easily made apparent by soaking the hair in liquor potassæ after washing in ether. The spores (which are twice the size of trico-

Digitized by Google

phyton spores and remarkably refringent) from mutual pressure are polyhedral, and together form a sort of tessellated mosaic, the elements of which seem to be held together by a greenish soluble cement in which a number of minute bacteria-like rods are incorporated. The shaft of the hair—not eroded or affected in any way—can be seen intact through the encrusting fungus. *T. giganteum* is easily cultivated on ordinary media. It liquefies gelatin in ten or twelve days. The smallest spores measure 2–5 μ, the largest up to 12 μ. Piedra is supposed by some to be induced by the mucilaginous hair applications in vogue among the Colombians.

Diagnosis.—Although Juhel-Rénoy has given to piedra the name "trichomycose nodulaire," the condition must not be confounded with trichomycosis nodosa, which is quite a different affection and common enough on the axillary, scrotal, and face hair in Europe and elsewhere. Neither must it be confounded with trichorexis nodosa, a non-parasitic disease of the hair-shaft, which is split up at different points into brush-like bundles of fibres and is thus easily fractured: nor with moniliform hair, a congenital, hereditary, and also non-parasitic disease.

Treatment. — Cleanliness, the free use of soap, and the application of some epiphyticide should suffice for cure; but should such means fail, doubtless shaving the scalp would be effectual.

Trichonocardiasis

Like trichomycosis, trichonocardiasis is a fungous disease of the hair in many ways resembling piedra, and common in Central Africa. It may produce skin irritation and staining of the clothes.

Fig. 210.—Trichonocardiasis. Human hair magnified. (*Wellcome Bureau of Scientific Research.*)

The shafts of the hairs, more especially those in the axilla, are attacked. The parasite is known as *Discomyces* (*Nocardia*) *tenuis* (Fig. 210). The hairs have a beaded or nodular appearance and the deposit may vary considerably in colour. The disease may spread to the skin and cause a severe intertrigo.

Treatment.—The affected hair should be bathed twice daily

Digitized by Google

with a lotion consisting of 1 dr. of formalin to 6 oz. of rectified spirit, reinforced by 2 per cent. of sulphur ointment.

IV.—SKIN DISEASES CAUSED BY ANIMALS

The Chigger, or Sand-Flea (*Dermatophilus penetrans*)

This insect, formerly confined to the tropical parts of America (30° N. to 30° S.) and to the West Indies, appeared on the West Coast of Africa for the first time about the year 1872. Since that date it has spread all over the tropical parts of that continent

Fig. 211.—Chigger (Dermatophilus penetrans), male. × 10 diam. (*Blanchard.*)

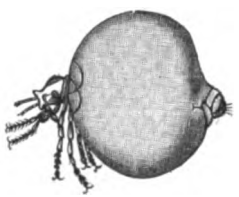


Fig. 212.—Chigger, impregnated female. × 10 diam. (*Blanchard.*)

and even to some of the adjacent islands—Madagascar, for example. As a cause of suffering, invaliding, and indirectly of death, it is an insect of some importance. It is now extremely prevalent on the East Coast of Africa, and is causing a large amount of invaliding amongst the Indian coolies there, by whom it has been introduced into India.

The chigger (Fig. 211) is not unlike the common flea (*Pulex irritans*) either in appearance or, with one exception, in habit. It is somewhat smaller in size (1 mm.), the head being proportionately larger and the abdomen deeper than in the latter insect. In colour it is red or reddish brown. Like the flea, its favourite haunt is dry, sandy soil, the dust and ashes in badly kept native huts, the stables of cattle, poultry pens, and the like. It greedily attacks all warm-blooded animals, including birds and man. Until impregnated, the female, like the male, is free, feeding intermittently as opportunity offers. So soon as she becomes impregnated she avails herself of the first warm-blooded animal she encounters to burrow diagonally into its skin, where, being well nourished by the blood, she proceeds to ovulation. By the end of this process her abdomen, in consequence of the growth of the eggs it contains, has attained the size of a small pea (Fig. 212). The first anterior and the two posterior segments do not participate in the enlargement, the latter acting as a plug to the little hole made by the flea on entering the skin. When the ova are mature they are expelled and fall on the ground. In a

Digitized by Google

short time a thirteen-ringed larva is hatched out from each egg. This larva presently encloses itself in a cocoon, from which, in eight or ten days, the imago emerges.

During her gestation the chigger causes a considerable amount of irritation. In consequence of this, pus forms around her distended abdomen, which now raises the inflamed integument into a pea-like elevation. After the eggs are laid (according to some,

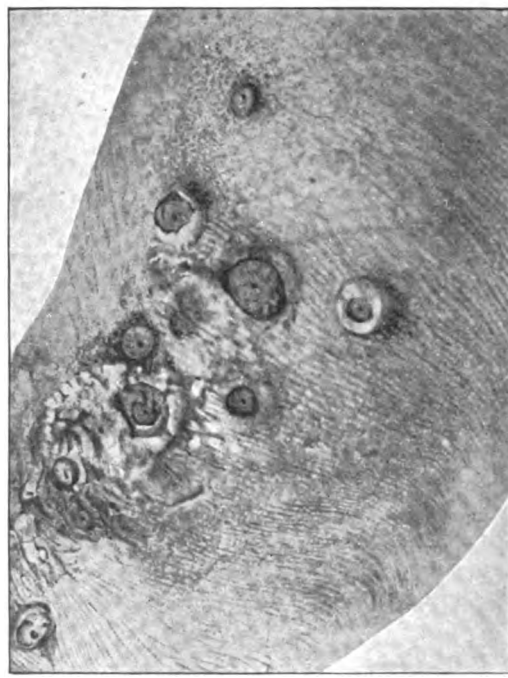


Fig. 213.—Chiggers in sole of foot. (*From a photograph by Daniels.*)

before this process) the superjacent skin ulcerates and the chigger is expelled, leaving a small sore which, if infected by any pathogenic micro-organism, as the bacterium of phagedæna or of tetanus, may lead to grave consequences.

Naturally, being nearest the ground, the feet are the parts most commonly infested by chiggers. The soles of the feet (Fig. 213), the skin between the toes, and that at the roots of the nails are favourite situations. Other parts of the body are by no means exempt; the scrotum, penis, the skin around the anus, the thighs, and even the hands (Fig. 214) and face, are often attacked. Usually

Digitized by Google

only one or two chiggers are found at a time ; occasionally they are present in hundreds, the little pits left after their extraction, or expulsion, being sometimes so closely set that parts of the surface may look like a honeycomb.

Treatment.—In chigger regions the houses, particularly the ground floors, must be frequently swept and accumulation of dust and débris be prevented. The housing of cattle, pigs, and poultry must be similarly attended to. The floors should be sprinkled often with carbolic water, pyrethrum powder, or similar

Fig. 214.—Chigger lesions of hands and feet. (*From a photograph by Daniels.*)

insecticide, and walking barefooted must be avoided. Bathing must be practised daily, and any chiggers that may have fastened themselves on the skin at once removed. They may be killed by pricking them with a needle, or by the application of chloroform, turpentine, mercurial ointment, or similar means, after which they are expelled by ulceration. The best treatment, however, is not to wait for ulceration, but to enlarge the orifice of entrance with a sharp, clean needle and neatly to enucleate the insect entire. Some native women, from long practice, are experts at this little operation. The part must be dressed anti-

Digitized by Google

septically and protected until healed. Europeans living in an endemic district should wear high boots. A daily inspection of the feet, especially under the nails, is advisable. Should any black dot be discovered, the chigger should be removed at once.

Prophylaxis.—Wherever possible, camps should not be formed in chigger-infested spots or in the neighbourhood of native villages. The camping-ground should be swept or, if necessary, fired; the floors of huts and tents may be sprayed with insecticides and naphthaline, and native tobacco dusted inside boots or shoes. Balfour recommends that the feet be rubbed thoroughly with a mixture consisting of 5 drops of lysol or liq. cresoli sap. in 1 oz. of vaseline. Special attention should be paid to the interdigital clefts.

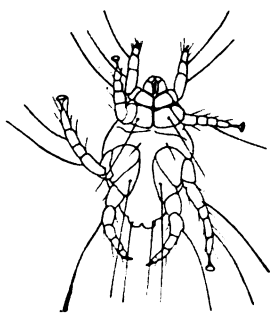


Fig. 215. — Pediculoides ventricosus, male. × 80 diam. (*After Alcock.*)

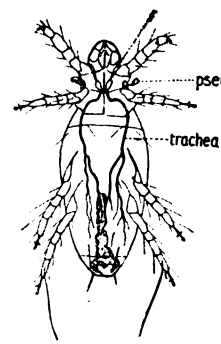


Fig. 216. — Pediculoides ventricosus, adult female. × 80 diam. (*After Alcock.*)

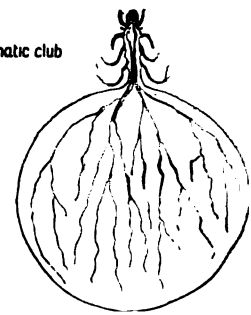


Fig. 217.—Pediculoides ventricosus, pregnant female with brood-sac. × 80 diam. (*After Alcock.*)

Acarine Dermatomycosis

Several forms of mites inhabiting sugar, grain, or copra may live as temporary parasites on the skin of man, and set up an intense irritation not unlike that produced by scabies. One of the most familiar of these is "grocer's itch," caused by the mites of the genus *Glycophagus*, which are common in raw sugar and cause an erythematous rash. Amongst the copra workers in Ceylon and the Pacific islands a similar skin affection is caused by a *Tyroglyphus*. "Grain itch," an urticarial and papular eruption of the exposed parts of the body, is caused by *Pediculoides ventricosus* (Figs. 215, 216, 217) in those who handle grain, cotton-seed, or beans. The presence of these mites causes a pruritus which is almost maddening. Preventive treatment consists in the application of beta-naphthol ointment (5 per

Digitized by Google

cent.), and the employment of dilute carbolic acid to kill off the mites.

Myiasis

The Screwworm (*Chrysomyia macellaria*)

This is the larva of a dipterous insect (Fig. 218) common in certain parts (especially the tropics) of America, from Canada to Patagonia, and has been

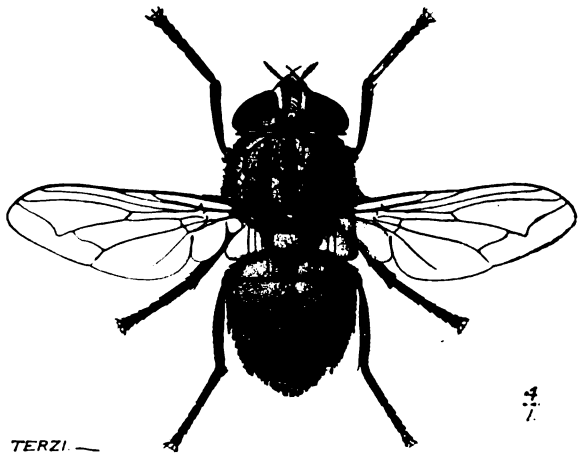


Fig. 218.—Chrysomyia macellaria, female.

reported from Cochin China. The insect (9–10 mm. long) lays a mass of three or four hundred eggs on the surface of wounds, and in the ears and nasal fossæ (Fig. 220) of persons sleeping in the open air, especially of those having offensive discharges which attract the fly. From these eggs the larvæ are hatched in a few hours. The larvæ (Fig. 219) are white, about

Fig. 219.—Chrysomyia macellaria, larva.

three-quarters of an inch in length, and formed of twelve segments carrying circles of minute spirally arranged spines which give the creature a screw-like appearance; hence the vulgar name. They burrow in the tissues, devouring the mucous membrane, muscles, cartilages, periosteum, and even the bones, thereby causing terrible sores, and not infrequently—particularly when they attack the ear or nasal fossæ—by penetrating to the brain, death. Of 13 cases collected by Laboulbène, 9 proved fatal; of 31 collected by Maillard, 21 died.

Digitized by Google

If treated properly and in time by injections of chloroform, carbolic acid, turpentine, infusion of pyrethrum, or a similar substance, the patient may be saved; neglected, he will most probably die. If necessary the frontal sinuses, the antrum, and other bony cavities must be opened to secure the expulsion of the larvæ.

In countries where this pest occurs, bloody and offensive discharges from the nostrils should be carefully investigated, and, if found to be caused by

Fig. 220.—Native with Chrysomyia macellaria in nostrils and frontal sinuses: early stage. (*From a photograph by Daniels.*)

the screwworm, vigorously treated. The fly is most active during the hottest part of the day, when the female deposits her eggs.

Ver Macaque (*Dermatobia cyaniventris*)

Synonym.—*Dermatobia noxialis.*

This is the larva of an American fly (Fig. 221) the identity of which, until it was studied by Blanchard, was doubtful. It is now known to belong to the family of Œstridæ.

At an early stage the larva has the appearance represented by Fig. 222; at a later stage, that represented by Fig. 223. The former stage of the larva is called *ver macaque*; the latter, much larger, *torcel* or *berne*. At one time

Digitized by Google

these two larval stages of the same insect were erroneously supposed to belong to different species.

Dermatobia cyaniventris measures from 14 to 16 mm. in length; it has a yellow head with very prominent brown eyes; the thorax is of a greyish colour, the abdomen of a dark metallic blue. It is widely distributed throughout tropical America, being especially common near wooded lands.

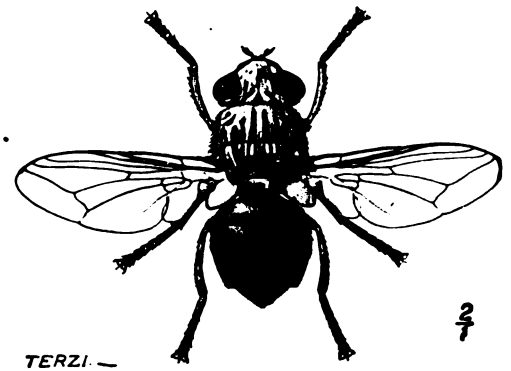


Fig. 221.—Dermatobia cyaniventris, female.

The larva occurs in the most diverse animals. It is found commonly in cattle, pigs, and dogs, but it occurs in the agouti, in the jaguar, in various monkeys, and in birds. It is rare in the mule, and writers have commented upon its absence from the horse. In man it has been reported from various

Fig. 222. — Dermatobia cyaniventris, larva: early stage. (*Blanchard.*)

Fig. 223.– Dermatobia cyaniventris, larva: later stage. (*After Brauer.*)

regions of the body, namely, head, arm, back, abdomen, scrotum, buttocks, thigh, axilla. Its presence is accompanied by excruciating pains, especially at those times when the larva is moving.

Blanchard, Surcouf, and Zepeda have recently thrown a curious light on the way in which this myiasis is acquired. It would appear that on attaining maturity *Dermatobia cyaniventris* lays its eggs on damp leaves in damp places, the haunts of a certain species of mosquito, *Janthinosoma lutzi* (Fig. 224).

Digitized by Google

The packets of eggs are enclosed in a cement which, on becoming softened by moisture, adheres to the mosquito's thorax, and the eggs are thus conveyed to man or other vertebrate when the mosquito next proceeds to feed.

It is supposed that when hatched out the larvæ penetrate the skin and produce an inflamed swelling about the aperture of entrance, from which a sero-purulent fluid, containing the black fæces of the larva, exudes.

Ver du Cayor (*Cordylobia anthropophaga*)

Synonyms.—*Ochromyia anthropophaga; Tumbu Fly.*

Cordylobia anthropophaga, one of the Œstridæ (Fig. 225), measures from 8·5 to 11·5 mm. in length. It is of a yellowish-grey colour, with black spots on the abdomen. It was first reported from Cayor, Senegambia, but it is probably widely distributed in tropical Africa. The larva (Fig. 226) burrows

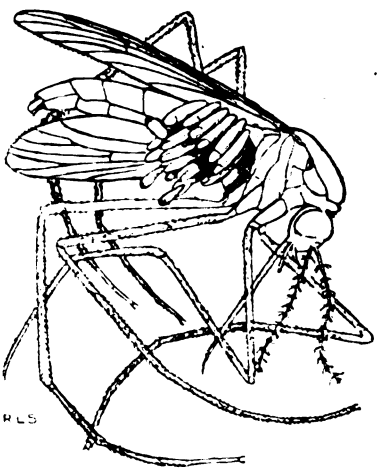


Fig. 224.—Janthinosoma lutzi carrying ova of D. cyaniventris.
(*By courtesy of the Tropical Diseases Bureau.*)

into the skin of man and beast—especially the forearm, scrotum, upper part of the thigh, and buttock—and produces a small inflamed swelling, from which it emerges in six to seven days.

The fly much resembles *Auchmeromyia luteola* (*see* below), but the male *Cordylobia* is distinguished from the male of that species by the closely-set eyes. In the female *Cordylobia* the abdominal segments are of equal size, while in the female *Auchmeromyia* the seventh segment is of greater length than the others.

In Africa, and in many other parts of the tropical world, similar anthropophagous larvæ, which, however, have not yet been satisfactorily identified, are frequently encountered. According to Grünberg all these larvæ belong to one species—*Cordylobia anthropophaga;* on the other hand, Gedoelst distinguishes four different species—*Ochromyia anthropophaga, Bengalia depressa* (widely distributed), *Cordylobia anthropophaga* (German East Africa), and a larva of undetermined species—Lund's larva (Congo Free State).

Digitized by Google

AUCHMEROMYIA LUTEOLA (Fabricius, 1805)

Synonym.—*Musca luteola.*

History.—*Auchmeromyia luteola* was first described by Fabricius in 1805 under the name of *Musca luteola.* In January, 1904, Lelean described and figured this fly, which he had collected and reared from the larva while on service with the Anglo-French Boundary Commission in Northern Nigeria. He stated that the larva occurs as a cutaneous parasite on natives near Sokoto. In July of the same year, at the Oxford meeting of the British

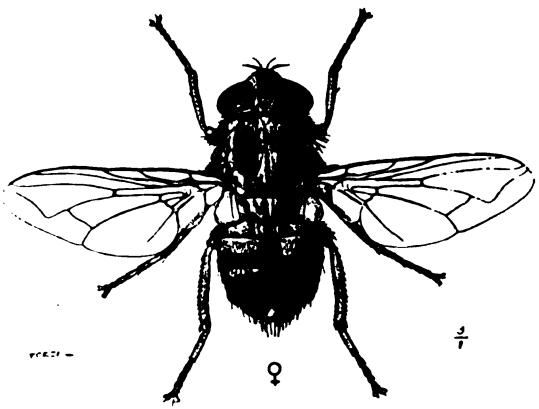


Fig. 225.—Cordylobia anthropophaga.

Medical Association, Dutton, Todd and Christy gave a more detailed account of the life habits of this dipterous insect, and pointed out that in its larval stage it is a keen blood-sucker, and is known throughout the Congo as the "Congo floor maggot."

Geographical distribution.—*Auchmeromyia luteola* is widely distributed

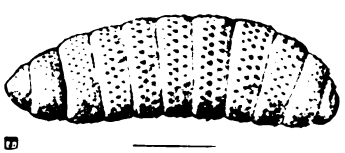


Fig. 226.—Cordylobia anthropophaga, larva.

throughout tropical Africa. It ranges from Northern Nigeria to Natal. Dutton, Todd and Christy found it all over the Lutete and surrounding districts, and at Leopoldville. They were told that it is common at San Salvador in Portuguese territory, on the Congo at Matadi in the cataract region, and at Tchumbiri, 150 miles above Stanley Pool. An intelligent native from Lake Tchad informed them that it was common in Western Tchad regions. It was found by Neave in the Sudan.

Specific diagnosis (Fig. 227).—The fly measures from 10 to 12 mm. in length, and its body is rather stoutly built. The general colour is orange-

Digitized by Google

buff, but numerous small black hairs give it a smoky appearance. The head is large, with eyes well separated in both sexes. The thorax shows two indistinct, dark, longitudinal stripes, which do not reach its posterior border. The abdomen differs in the two sexes, the second segment in the female being twice the length of the same segment in the male. The first segment has a narrow dark stripe on its posterior margin in both sexes; the second segment in the male is marked by a broader band, tapering forwards along the middle line to the base of the segment. In the female the dark band is so wide that

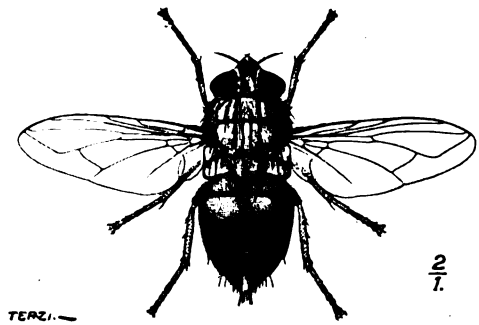


Fig. 227.—Auchmeromyia luteola, female.

it occupies almost the whole segment. The third segment is almost entirely black in both sexes. The fourth is dark at the base and lighter posteriorly. The legs are the same colour as the rest of the body. The first tarsal joint is jet-black, and stands out prominently against the large cream-white pulvillus. The wings are of a smoky-brown colour with conspicuous venation.

The larva (Fig. 228) is of a dirty-white colour and semi-translucent. It

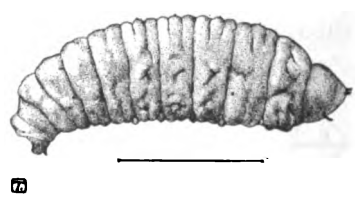


Fig. 228.—Auchmeromyia luteola, larva.

consists of eleven distinct segments, and when fully grown measures about 15 mm. in length. The central part of the ventral surface is flattened. At the posterior margin of each segment are three short limbs transversely arranged and provided with spines directed backwards. These enable the maggot to move about caterpillar-like and fairly rapidly. Laterally the segments bear two or more irregular protuberances, each of which has a posteriorly directed spine and a small pit. The anterior segment is roughly conical, and bears the mouth, which is placed between two black hooks protruding from its apex and curved backwards towards the ventral surface of the body. Paired groups of minute teeth are placed around the two hooks

Digitized by Google

so as to form a sort of cupping apparatus. The last segment is larger, depressed, and turned upwards at an angle of about 45° with the rest of the body; two spiracles open on its dorsal surface surrounded by spines. The anus is placed in the anterior portion of its ventral surface, and behind it are two prominent spines. The alimentary canal commences with a short œsophagus, which ends in a proventriculus. A remarkable dorsal diverticulum, corresponding to the food reservoir of the muscid larva, opens into the œsophagus near its anterior end. After the larva has fed, the diverticulum is a very conspicuous object, being seen through the semitransparent body-wall as a bright-red area, extending, when full of blood, from the head to about the fifth segment. The midgut is short; the hindgut is long, much coiled, and occupies the greater part of the body cavity. The maggot has a thick integument, which enables it to withstand a good deal of pressure without injury.

The duration of the larval period has not been determined. When ready to pupate, the larva selects a suitable spot and lies dormant. The puparium is a dark reddish-brown oblong body, measuring 9–10·5 mm. in length by 4–5 mm. in breadth. The anterior end is roughly conical; the posterior is rounded. The pupa stage lasts from two to three weeks.

The fly is usually found sitting motionless amongst the thatch, beams, and cobwebs of the walls and roofs of native huts, but it is very difficult to see on account of its protective colouring, which corresponds exactly with the smoke-stained straw and rafters. It never bites, is usually silent, and deposits its eggs in the dust-filled cracks and crevices of the mud floors of the huts, particularly in spots where urine has been voided.

The larvæ are found especially under the mats on which the natives sleep, in the floor crevices, and in moist soft earth at a depth of 3 in. or more. According to Bentley, as many as fifty could sometimes be found beneath a single mattress. They feed mainly or entirely at night, and they drop off at once if the limb on which they are feeding is moved. Those who sleep on beds or raised platforms are not attacked, as a rule, unless the bed be low, when the maggot may reach the occupant by crawling up either the supports or the grass wall against which the bed is usually placed. The natives state that the maggot is able to jump to a height of 18 in., but this is unlikely.

The larvæ of these anthropophagous flies may be recognized by the characteristic shape of the stigmata at the posterior extremity (Fig. 229).

Larva Migrans

Synonyms.—Myiasis Linearis; Creeping Eruption; Dermatitis Linearis Migrans.

This condition, first described by Lee in 1874, and at a later period by Crocker, is said to be common in Russia; certainly it is not infrequent in the tropics, especially in Ceylon. It appears to be due to the burrowing of a larva—probably one of the Œstridæ, or gadflies—under the epidermis. These larvæ have been identified as belonging to the genera *Gastrophilus*, *Œstromyia*, and *Hypoderma*. Looss has stated that the same effects may be produced by the larva of *Ankylostoma* and, it may be, of *Strongyloides* as well.

The manner in which the larva enters the skin is unknown. Unlike the itch-mite, it burrows on indefinitely, like a mole, and forms a red line or narrow raised ridge ¼ in. broad. The parasite appears to travel at the rate of ½–1 in. in twenty-four hours. The line zigzags and twists about, but does

Digitized by Google

not bifurcate, and may be found in any part of the body—the face, chest, or more particularly the soles of the feet and the legs. While the advancing end of the line progresses the opposite end fades away. The only subjective symptom is itching. The duration of the disease may be very long.

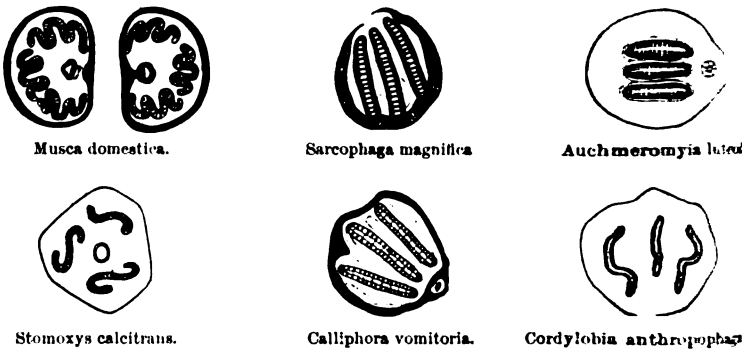


Fig. 229.—Stigmata of muscid larvæ, a means of rapid identification. Magnified.

Treatment by injection of cocaine and parasiticidal substances in advance of the migrating larva has so far proved to be unsatisfactory.

Leeches

In the grass and jungle lands of many tropical and subtropical countries land-leeches, probably of special species, often occur in great abundance; so much so that in some circumstances they may prove to be something more than a nuisance. The *Hæmadipsa zeylanica* is one of the most active, as well as best known, of these. Before feeding, when outstretched, it is about an inch in length and about the thickness of a knitting-needle. It clings to a leaf or twig, awaiting the passing of some animal, on to which it

Fig. 230.—Limnatis nilotica. Half nat. size. (*Sheppard, del.*)

springs with remarkable activity. It at once attaches itself to the skin and proceeds to make a meal on the blood. Animals are sometimes killed in this way; men even have been known to succumb to the repeated small bleedings by these pests. It is necessary, therefore, when passing through jungle lands in which leeches abound, to have the feet and legs carefully protected. The bite is not infrequently the starting-point of a troublesome sore.

In the South of Europe and in the North of Africa the horse-leech, *Limnatis nilotica* (Fig. 230), sometimes gets into the gullet and nostrils of men as well as of animals. It has occasionally caused death by entering and occluding the

Digitized by Google

air-passages. These leeches are a source of inconvenience to French troops in Algeria, and are mentioned as occurring in Napoleon's army in its retreat through the Sinai Peninsula; and several cases were noted among British troops during the late Egyptian and Palestine campaigns. In Formosa Manson heard of and saw several instances of a similar form of parasitism, both in men and in monkeys. To what particular species the leech in these cases belonged is not known. Doubtless, when very young the leeches were taken in unperceived with foul drinking-water, and, wandering round the soft palate, found their way into the nose. Occasionally, in the cases referred to, the animals would protrude from the nares and wander over the upper lip. For a long time they contrived to elude all attempts at capture. By dipping the face in cold water they could generally be persuaded to show themselves. In one instance the leech dropped out spontaneously. In another—an American naturalist who had been travelling much in the interior of Formosa, and who had suffered from severe headache and profound anæmia, the results of repeated epistaxis—Manson succeeded in removing the leech by attaching through a speculum a spring forceps to its hinder end, and afterwards injecting salt and water. It would be well to bear in mind that in tropical countries persistent headache, associated with recurring epistaxis, may be caused by a leech in the nostril. (*See also* Appendix II., p. 851.)

Digitized by Google

Section VIII.—LOCAL DISEASES OF UNCERTAIN NATURE

CHAPTER XLVIII

CRAW-CRAW—CHAPPA—CLIMATIC BUBO—GOUNDOU —AINHUM—BIG HEEL—ONYALAI

Craw-Craw and Ulcerating Dermatitis

Synonym.—Nodular Dermatitis.

Most itching papular and pustular eruptions are termed kra-kra by the natives of the West Coast of Africa. O'Neil describes under this name a pustular affection which he says is common in certain parts of the West Coast, and which he found to be associated with the presence of a filariform parasite in the papules; this form of craw-craw resembles scabies; but he adds that symptoms subside in a cooler climate—to return, however, when the negro revisits the hot and damp atmosphere of his native country. The papules occur all over the limbs and body, either singly or in rings. In two days from its appearance the papule becomes a vesicle, and in two more a pustule.

In the exudate obtained from these papules O'Neil found small filariform embryos which resembled *microfilaria perstans*. The question of the filarial origin of craw-craw has again been raised by Montpellier and Lacroix, who claim to have found adult filariæ in the lesions; but Brumpt does not believe that these are examples of *Onchocerca volvulus*, as has been affirmed.

Craw-craw is said to be contagious. It appears after an incubation period of three days, and is not curable by sulphur inunction.

Symptoms.—The term craw-craw is very loosely applied. Emily has described under this name a papulo-pustular skin affection which is common in certain parts of tropical Africa and is often the cause of much suffering to the traveller. It, or a similar disease, is by no means confined to Africa, for it is seen in patients from Ceylon and India, and Manson was at one time very familiar with it in South China. At the earliest stage the disease begins as an itching papule, very possibly at the seat of a mosquito-bite. The itching provokes scratching, whereby some

Digitized by Google

form of pyogenic micro-organism is inoculated. Pustulation follows, and is spread over feet and legs by soiled shoes and stockings and auto-inoculation. In this way an ulcerating, pustulating dermatitis is kept up. Cantlie's "foot-tetter" is of this nature. Plehn describes the disease as a chronic folliculitis of the skin. The organism which causes the suppuration appears to be *Staphylococcus pyogenes aureus*.

Diagnosis.—The hard horny papules of craw-craw have to be differentiated from scabies, which is common in African natives.

Treatment.—Emily describes a very efficient treatment. Pustules are opened, crusts removed, and ulcers scraped. Boric-acid powder is then dusted freely on the parts after a thorough scrubbing with sublimate lotion (1 : 1,000), boricated vaseline is applied on lint, and over all absorbent cotton and a bandage. The dressings are not disturbed for a week, when the parts will be found soundly healed. Similar auto-infective diseases, so common in the tropics, may be treated by prolonged soaking in a warm carbolic-acid lotion (1 : 20), followed by dry dressing with boric powder. Infected slippers, shoes, and stockings should be destroyed.

Chappa

Under the name "chappa" Read described a disease which he met with near Lagos, Nigeria. During two and a half years he saw six examples—two in males, four in females. He thus described it :—

"The patients all give the same history. The disease commences with severe pains in the limbs, muscles, and joints. After a few months the pain decreases, and some joints begin to swell and convey the sense of fluctuation. About the same time nodules develop in different parts of the body. These nodules are in the subcutaneous tissue, and are about the size of a pigeon's egg. After a time, without the formation of an abscess, the skin over the nodule ulcerates and exposes a circular or oval ulcer with a fatty-looking base. The nodules may be single, but are more often multiple, and may be so close together that when ulceration ensues the ulcers coalesce, forming a serpiginous ulcer. Sometimes the nodules are absorbed without proceeding to ulceration. The ulcers are very chronic and last for years, sometimes healing at one place and gradually extending in another. The joints I have seen most affected are the knee, elbow, and wrist. The sense of fluctuation was so marked in one case that I opened the joint; but no fluid exuded, a fatty-looking material protruding through the incision. The disease after a time attacks the bones, and the joints may become totally disorganized."

Possibly the same disease occurs in British East Africa under the name of "acropathia mutilante." Guiteras has described similar lesions in Europeans in Cuba.

Digitized by Google

Treatment.—Neither potassium iodide nor mercury avails. Scraping, escharotics, and antiseptics seem to be more effective; but, although the disease may heal under treatment in one place, it breaks out in another.

Climatic Bubo

Scheube applied the term "climatic bubo" to a type of non-venereal adenitis not uncommon in tropical climates. So far as available statistics show, the disease is especially prevalent among the crews of warships on the eastern coast of Africa. It occurs also in the Straits of Malacca, in China, in the West Indies, Japan, the Mediterranean, and probably in many other places, including, perhaps, in a minor degree, Europe. It appears to be epidemic at times in certain places, and to prevail in groups of individuals living under similar hygienic conditions.

The pus from a climatic bubo is almost invariably sterile. Garrow has isolated a Gram-negative bacillus from the blood in the acute febrile stage, resembling a paratyphoid organism and agglutinating in high titre with the patient's serum. It may be that the adenitis depends on some virus which has been introduced through an overlooked wound or insect bite on the legs or genitals.

Diagnosis has to be made from venereal bubo, filarial adenitis, and plague. None of these diseases should cause any real difficulty.

Symptoms.—The disease generally commences with fever of a remittent type in association with inflammatory swelling, usually of a subacute character, of the groin glands. The oblique inguinal glands are those most frequently affected, but at times it is the crural glands that are attacked. Sometimes both groins are affected, sometimes only one, sometimes one groin is attacked after the other. The affected glands slowly or more rapidly enlarge to the size of a hen's egg, or even larger. After several weeks, it may be months, the swelling gradually subsides. Occasionally the periglandular connective tissues inflame, the integuments become adherent, and suppuration ensues. If the suppurating glands be freely incised, or excised, the parts readily heal; but if they are left alone, or inefficiently treated, fistulous tracks form and may take a very long time to heal.

Treatment should consist in rest and soothing applications during the more acute stage. After pain and tenderness have

Digitized by Google

subsided, graduated elastic pressure should be applied; X-rays have been recommended. Concurrent malaria would call for quinine; syphilis, for mercury or the iodides.

GOUNDOU, OR ANÁKHRÉ ("GROS NEZ")

In 1882 MacAlister drew attention to what were termed the horned men of Africa, and in 1887 Lamprey gave further details illustrated with drawings. Maclaud called attention to what is manifestly the same affection, which, according to him, occurs in a considerable proportion—one or two per hundred—of the inhabitants of certain villages on the Ivory Coast. The natives call it *goundou* and also *anákhré*. Later observations show that it has a considerably wider distribution in Central Africa and South America, and that a similar disease occurs in the larger apes, chimpanzees, and baboons.

Symptoms.—The disease usually commences soon after child hood, although adults also may be attacked. The earliest symptoms are severe and more or less persistent headache which, after a time, is associated with a sanguino-purulent discharge from the nostrils and the formation of symmetrical swellings the size of a small bean at the side of the nose. Apparently the swelling affects the nasal process of the superior maxilla. The cartilages are not involved. After continuing for six or eight months, the headache and discharge subside. Not so the swellings; these persist and continue slowly and steadily to increase until in time they may attain the size of an orange, or even of an ostrich's egg. As they grow, the tumours, encroaching on the eyes, may interfere with the line of vision and finally destroy these organs. There is no pain in the tumours themselves. The superjacent skin is not involved, being healthy-looking and freely movable. The tumours are oval, with the long axes directed downwards and slightly from within outwards. The nostrils are bulged inwards and more or less obstructed. The hard palate is not affected in any way.

In the case of a West Indian child (Fig. 231) reported by Strachan the swellings were congenital, and had only increased in proportion to the child's growth. They were hard, smooth, bony masses, somewhat of the shape and size of an elongated pigeon's egg, and sprang from the nasal process of the superior maxillary and nasal bones.

Chalmers has given an account of this affection as seen on the Gold Coast, where it is fairly common and is known as "henpuye." *

* Henpuye = dog nose anákhré = big nose: native names applied to the disease.

Digitized by Google

The bony outgrowths, not necessarily bilateral, are attached to the nasal bone and nasal process of the maxilla, but according to Botreau-Roussel and Clapier, in recent papers, they are not

Fig. 231.—Goundou in a West Indian child. (*Dr. Henry Strachan.*)

entirely confined to this region, as similar hyperostoses may coexist on the tibia, upper or lower jaw, forearm, femur, or clavicle.

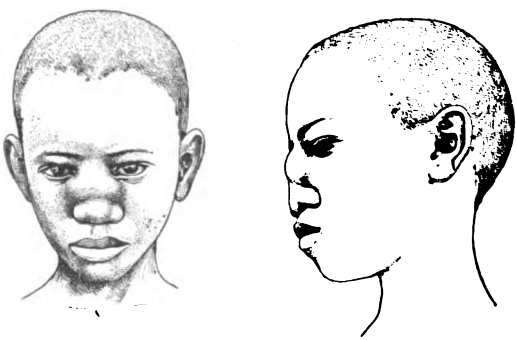


Fig. 232.—Goundou. ("*Journ. Trop. Med.*")

The latter is of the opinion that goundou is a systematized hypertrophic osteitis arising from yaws.

Treatment consists in incising and displacing the periosteum and chipping away the bony outgrowth with a chisel.

Digitized by Google

Juxta-Articular Nodules (Fig. 233)

First described in 1901 by Macgregor, and subsequently named by Jeanselme, these fibrotic tumours are now known to occur in the natives of many tropical countries, as Java, Siam, Madagascar, and, especially, tropical Africa. The nodes are situated most frequently over the olecranon, great trochanter, external malleolus, acromion, lower end of femur, or upper end of tibia. In Africa, owing to concurrence in tropical distribution and similarity in appearance, they are apt to be mistaken for *Onchocerca volvulus* cysts (p. 637), and vice versa. In both cases the swellings are originally subcutaneous; they increase in size very slowly, and may attain the dimensions of a small orange; they are round or oval, and firm in consistence. They are painless, and very rarely ulcerate or suppurate. The juxta-articular nodules are generally multiple; they occur, as the name implies, in the neighbourhood of joints, occasionally on the external surfaces of limbs, and are arranged symmetrically. They are of a woodeny hardness in contrast to the elastic firmness of the volvulus tumour, and, unlike the latter, of a somewhat irregular outline. In case of any doubt, diagnosis may be readily cleared up by aspirating the tumour with an exploring needle. A volvulus tumour will yield a viscid yellowish or turbid fluid containing microfilariæ; a juxta-articular nodule yields no fluid or, at most, a drop of clear serum. At times, though rarely, the tumours disappear spontaneously. If they are inconveniently located they may be excised.

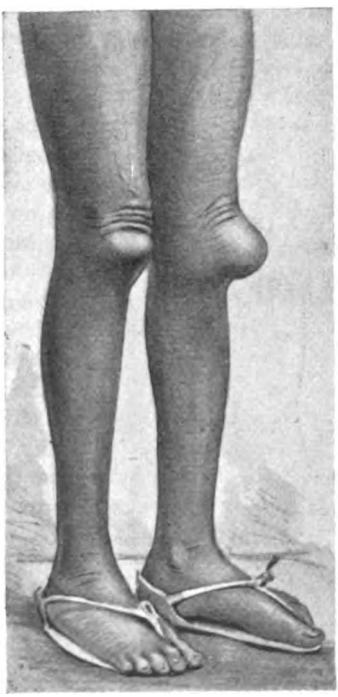


Fig. 233. — Juxta-articular nodules. (*Photo: Dr. Watts.*)

Macgregor and others considered that these tumours were of parasitic origin, and Fontoynont and Carougeau claim to have discovered the parasite as an extremely delicate fungus, *Nocardia*

Digitized by Google

carougeaui. Clapier, who has given much attention to, and has had long experience of, the tumours in French Guinea, failed to confirm this claim. On the other hand, Davey in Nyasaland and Mouchet and Dubois on the Congo, regard them as a late manifestation of yaws.

AINHUM

This is a disease of a very peculiar character, affecting the toes, particularly the little toes, of negroes, East Indians, and other dark-skinned races, both in the Old and New Worlds. The name, derived from the Nago dialect, means "to saw or cut."

Symptoms.—The disease commences as a narrow groove in the skin, almost invariably on the inner and plantar side of the root of the little toe. It may occur in one foot only, or in both feet simultaneously, or it may affect one foot after the other. The groove, once started, deepens and extends gradually round the whole circumference of the toe. As it deepens—it may be, though not necessarily, with some amount of ulceration—the distal portion of the member is apt to swell to a considerable size, as if constricted by a ligature. (Fig. 234.) There is little or no pain, although there may be inconvenience from the liability to injury to which the dangling and now everted toe is exposed. In the course of years the groove slowly deepens, and finally the toe drops off or is amputated. The groove may either correspond with a joint or it may be formed over the continuity of a phalanx. In rare instances, after the two distal phalanges have dropped off or been amputated, the disease recurs in the stump, and the proximal phalanx in its turn is thrown off. Of the other toes, the fourth is the one which is most frequently affected; very rarely is the third, or second, or great toe attacked. In the Army Medical Museum at Washington, U.S.A., there is a wax model representing a case of this or a similar affection, in which all the toes had been thrown off and the disease was making progress in the leg.

Fig. 234.—Ainhum.

Ainhum is very rare in women or children, being most common in adult males. It runs its course in from one to ten or even more years.

On section it is found, as a rule, though not invariably, that the panniculus adiposus of the affected toe is much hypertrophied,

Digitized by Google

that the bone is infiltrated with fatty matter, and that the other tissues are correspondingly degenerated. Sometimes the bone is thinned, or even altogether absorbed. At the seat of constriction a line of hypertrophy of the epithelial layers, and of atrophy of the papillary layer of the skin, together with a band of fibrous tissue more or less intimately connected with the derma, surrounds, in whole or in part, the narrow pedicle.

Nothing is known as to the true nature and cause of this disease, to which the European and white-skinned races are not, but to which the African races, particularly the negroes of the West Coast, are especially liable. Some have suggested that it is a trophic lesion depending upon some nervous affection. The occurrence of severe loin pains, which Dupouy says he remarked at the commencement in some of his cases, as well as the tendency of the affection to run in families, as noted by Da Silva Lima, affords a certain amount of support to this view. Others suggest that it is a manifestation of leprosy; others, that it is a form of sclerodermia; others again, and on equally inadequate grounds, that it is produced artificially by intentional ligation or by the wearing of toe-rings. Manson's impression is that it is provoked, at all events in the first instance, by wounds—so easily inflicted on bare feet in walking through grass or jungle. The fold of skin in which the lesion of ainhum commences is very liable, especially in the splayed-out toes of the negro, to be wounded in this way. If we examine the under-surface of the joint flexures of the toes in many individuals of this race, even of those not affected with ainhum, we often find the skin, particularly at the proximal joint of the little toe, thick, rough, scaling, and sometimes even ulcerated. One can understand that continual irritation of this sort, produced and kept up by wounds from sharp grasses or chiggers (Wellman), would in time give rise, especially in the dark-skinned races so prone to cheloid, to fibrotic changes in the derma, which might very well end in a sort of linear cicatricial contraction, and ultimately in slow atrophying strangulation of the affected member. The disease is said, however, to have been seen in those who wear shoes; but, unless it could be shown that such individuals had always worn shoes, this objection to the explanation offered would not apply. Manson saw a negro in whom the entire integument of the little toe was involved in a sclerodermia, and the part in consequence was shrunken and hidebound, whilst the little toe of the other foot was affected with well-marked ordinary ainhum; the process was diffuse, as it were, on the one side, localized on the other.

The tail in certain species of monkey is liable to a similar

Digitized by Google

disease. Manson had under observation for some time a pet monkey in which the part corresponding to the distal vertebra dropped off in consequence of an ainhum-like linear constriction. Two months later the next vertebra was similarly amputated, and later a third groove formed a little higher up the tail.

Treatment.—It has been suggested that division of the constricting fibrous band would delay the evolution of the disease. In the early stage this might be tried. When troublesome, the affected toe should be amputated.

Big Heel, or Endemic Hypertrophy of the Os Calcis

Maclean described a peculiar form of enlargement of the os calcis which he observed at Kaziankor, Gold Coast, West Africa, among Fantis and Kroos. The disease begins somewhat suddenly, being preceded by fever, and attended by pain and tenderness which reach their maximum in about a month, gradually diminishing during the succeeding one or two months. Concurrently with the pain a swelling of the external surface of the os calcis, rarely of the tarsal bones, makes its appearance. Sometimes one heel only, sometimes both heels are affected. The swelling may be so considerable as to be quite evident both to touch and sight. It subsides to a certain extent, though not altogether, as the pain diminishes. Locomotion is seriously interfered with by the pain, but there is no implication of joints. The disease relapses from time to time, more especially during the rainy season. In one case recorded by Maclean severe pain would be provoked by application of cold water.

Maxwell has reported a similar condition in natives of Formosa. As in Maclean's cases, the patients were young adults from 20 to 25 years of age. In Maxwell's cases the disease, although very painful, seemed to be of a more chronic character. In one instance the patient's sufferings were much relieved by trephining the affected bones. This curious condition somewhat resembles goundou. So far, we have no clue to its etiology. It is probably not syphilitic. Iodide of potassium did not relieve Maxwell's cases.

Onyalai

Yale Massey described under the above title a peculiar disease occurring among the natives of Portuguese West Africa. It has since been recognized in East Africa and on the Congo. It is characterized by the formation of a number of vesicles, distended with blood, from ¼ to ½ in. in diameter, on the hard palate and on the inside of the cheeks. Some of the vesicles are umbilicated.

Digitized by Google

They differ from ordinary blood blisters by the presence of numerous trabeculæ and the semi-coagulation of the contents; this makes the vesicle difficult to empty. The urine apparently invariably contains free blood. Numbness and pains in various parts of the body may be noted. There may be mental confusion; and the parotids may be swollen and tender. Occasionally the disease is accompanied by fever, and although with one exception all Yale Massey's cases recovered within a week to ten days, the natives regard the disease with dread owing to its reputation for deadliness. The etiology is quite unknown, though Mense has suggested that it is due to some kind of plant poisoning. The diagnosis has to be made from snake-bite in which hæmorrhagic symptoms supervene.

Massey recommends large doses of bicarbonate of soda and cod-liver oil as the best form of treatment.

Digitized by Google

APPENDIX I

MEDICAL PROTOZOOLOGY

THE **Protozoa**, which play such an important part in the etiology of tropical diseases, are unicellular organisms possessing a nucleus distinct from the cytoplasm. They belong to the Protista, a group of organisms including the simplest and most primitive forms of life, and which may be considered equivalent in systematic value to the animal and vegetable kingdoms.

The protozoal cell constitutes an entire individual; it may exist singly, or combined in the form of cell colonies.

The body is a mass of protoplasm, sometimes enclosed in a limiting envelope. Such organs as are present are also, for the most part, protoplasmic, and are used for the purposes of locomotion, capture of food, etc.

Reproduction takes place by fission. Sexual reproduction may also occur, and, as compared with other Protista, the developmental cycle may be a very complicated one assuming totally different forms at different periods of development.

There are certain forms of development in some of the protozoa, such as the Hæmosporidia, which it is necessary to define and for which certain terms are used. Their application, however, when loosely used has given rise to much confusion. The protozoa parasitic in blood of the vertebrate host undergo an asexual multiplication, the process being known as *schizogony*; but in order to ensure the existence of the organism, and its passage from one vertebrate host to another, a further cycle in an invertebrate host is necessary. This is a sexual cycle—*sporogony*, as it is termed.

In the vertebrate blood the young parasite is known as a *schizont*. The products of the asexual fission are known as *merozoites*; these merozoites at some period of their existence develop into forms known as *gametocytes*, destined to pass into the alimentary tract of the invertebrate host.

These gametocytes are quiescent until they are removed from the blood; when this occurs they develop into *gametes*. The *microgametes* formed in the male cell function as spermatozoa, enter and fertilize the female cell (*macrogamete*), thereafter known as a *zygote*.

After this act the zygote, in the Sporozoa, becomes an elongated motile body (*oökinete* or travelling vermicule), which ultimately becomes encysted (*oöcyst*). The oöcyst gives rise to secondary bodies in its interior (*sporoblasts*), which in turn develop into a number of minute filaments known as *sporozoites*. Usually these sporozoites contrive to enter the mouth of the insect, and by this route they gain access to the blood of a vertebrate host.

The Protozoa are generally divided into four main classes.

Class I.—SARCODINA

Protozoa in which the protoplasmic body has no limiting envelope in the form of a more or less rigid cortical layer, thus tending to a spherical shape in the passive forms, or an irregular, ever-changing shape in the creeping

Digitized by Google

forms. Organs serving for locomotion and capture of food are known as *pseudopodia*. A skeleton or shell may be present. Encysted resistant forms may also occur. Division into two is the usual method of multiplication.

EXAMPLES: *Entamœba coli, Entamœba histolytica.*

Class II. —MASTIGOPHORA

Protozoa in which the organs of locomotion are *flagella*, that is to say, long slender filaments capable of performing lashing movements. Certain blood parasites belong to the order Hæmoflagellata.

EXAMPLES: *Trichomonas, Giardia, Trypanosoma, Leishmania.*

Class III.—SPOROZOA

Protozoa occurring as blood or intracellular parasites of other organisms. They possess no definite external organs for locomotion or for ingestion of food. The typical reproduction takes place by the formation of spores containing minute germs called *sporozoites*. This class is divided into the orders Coccidia and Hæmosporidia.

EXAMPLES: *Coccidium, Plasmodium, Gregarina.*

Class IV.—CILIOPHORA

Protozoa in which small filaments called *cilia* serve as organs of locomotion; these are distinguished from flagella by their much smaller size and in being present in great numbers, sometimes forming a fine covering over the whole of the body. The body protoplasm is always corticate.

EXAMPLE: *Balantidium.*

CLASS I.—SARCODINA

This class, sometimes termed the Rhizopoda, includes parasitic amœbæ as well as free-living forms such as the Radiolaria and Foraminifera; these latter are of little interest to the student of tropical medicine. They are capable of independent amœboid locomotion by the alternate protrusion and retraction of protoplasmic processes called "pseudopodia."

Entamœba histolytica,* Schaudinn, 1903 (emend. Walker, 1911) (Fig. 235), the pathogenic amœba of man, has been considered in some detail in the text (p. 433), but a short summary may be given here. These amœbæ vary much in size and, as a rule, measure from 20–30 μ in diameter. When active they eject characteristic hyaline pseudopodia. The protoplasm of the organism is divisible into two zones—an outer clear ectoplasm and a granular endoplasm. The nucleus, which is generally invisible in the living state, has a characteristic structure, as is shown in the accompanying figure (Fig. 235, 1). Vacuoles are not present in healthy living individuals, though they may appear as bubbles in the protoplasm immediately after death. The large active entamœbæ live in the intestinal wall at the bases of the lesions they give rise to, and there undergo binary fission. They ingest red blood-corpuscles, leucocytes, and other portions of the tissues in which they live; this habit serves as a distinguishing feature between *E. histolytica* and the non-pathogenic amœbæ.

Cysts.—According to Wenyon and O'Connor, Dobell and Jepps, there are different races of *E. histolytica*, distinguishable by the size of their cysts

* *E. histolytica* is synonymous with *E. dysenteriæ*, Craig, 1905, and *E tetragena* (Vicreck), Hartmann, 1908.

Digitized by Google

(Fig. 235, 2–5). The smallest measure 7–9 μ in average diameter, the largest about 15 μ. The mature cyst is quadrinucleate, and very commonly contains within its substance refractile *chromatoid bodies*; a glycogen mass is usually also present and becomes evident upon the addition of iodine solution. The nuclei within the cyst retain the same characters as in the vegetative form.

Entamœba coli (Grassi, 1879), Casagrandi and Barbagallo, 1895 (Fig. 236).—After a period of great uncertainty and doubt, *Entamœba coli*, on morphological and pathological grounds which can no longer be questioned, emerges as a species distinct from *E. histolytica*. It is the largest amœba of man, though subject to great variation in size. The vegetative stage of

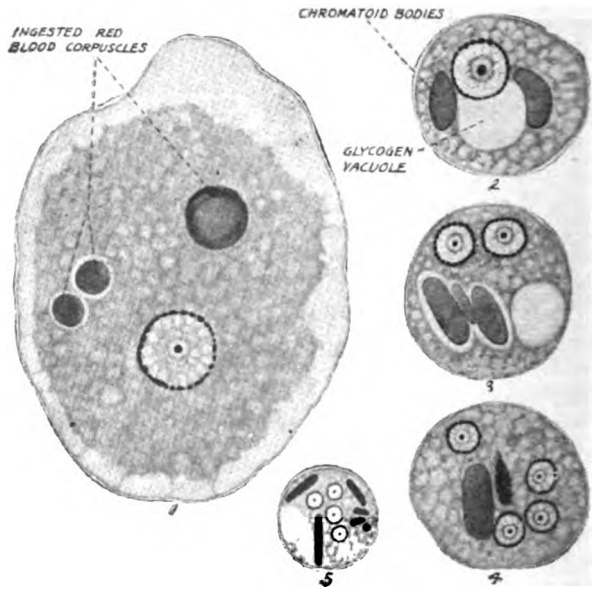


Fig. 235.—Entamœba histolytica. × 2,500 diameters. (*After Dobell.*)

1, Active amœboid form with ingested red blood-corpuscles; 2, uninucleate cyst; 3, binucleate cyst; 4, quadrinucleate cyst; 5, quadrinucleate cyst, small race, 6·6 μ in diameter.

the organism may vary from 18–40 μ; as a rule it is 20–23 μ in diameter. Its movements are more sluggish than those of *E. histolytica*; the sudden extrusion of pseudopodia is never seen. There is not the same differentiation of the cytoplasm, which is bulky and granular and usually charged with food vacuoles and various objects such as bacteria, but never with red blood-corpuscles or tissue elements. *E. coli*, in fact, leads a commensal existence in the fæces of the large intestine and does not prey upon the bowel wall

The nucleus is very large and conspicuous, easily visible in the unstained state, and composed of a definite thin nuclear ring and a comparatively small excentric karyosome. Definite chromatic granules are generally present in the area between the karyosome and the peripheral chromatic ring. Though these nuclear distinctions are constant in perfectly fresh

Digitized by Google

specimens, they lose their characters in individuals which are in the least degenerate.

E. coli generally shows vacuoles resembling fissures containing a liquid which may be water. The cytoplasm is greenish in colour, usually due to contained inclusions—these may often be of large size; and it may even ingest cysts of other protozoa, such as *E. histolytica*, *Giardia*, or coccidial cysts of the genus *Isospora* (Wenyon and O'Connor). (Fig. 237.) Starch grains, vegetable débris, and bacteria of all sorts form its customary food.

Like other entamœbæ, *E. coli* reproduces by binary fission, but no process of schizogony has ever been satisfactorily demonstrated. Like *E. histolytica*, before encystation the amœbæ undergo a considerable reduction in size.

Cysts.—The cysts (Fig. 236, 1) exhibit a considerable variation in size, 10–30 μ; and there is little doubt that, like *E. histolytica*, *E. coli* is a

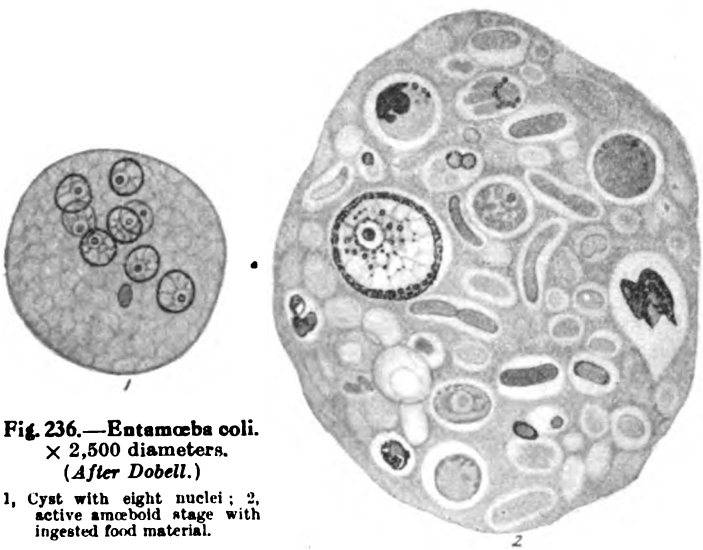


Fig. 236.—Entamœba coli. × 2,500 diameters. (*After Dobell.*)

1, Cyst with eight nuclei; 2, active amœboid stage with ingested food material.

composite species, consisting of a number of races distinguishable by the dimensions of their cysts. The resting nuclei within the cyst bear the same characters as does the vegetative form. At first uninucleate, they divide by binary fission into two, four, and eight, progressively diminishing in size as they do so. The mature cyst is octonucleate, though it must be remembered that immature quadrinucleate cysts occur, and occasionally supernucleated cysts with sixteen nuclei. The cytoplasm of the cyst contains a variable amount of glycogen, which is most abundant in the binucleate form and may be demonstrated with iodine solution. Chromatoid bodies are not always present, appearing more generally as small granular or rod-like bodies, especially in the binucleate stage. In mature octonucleate cysts they are, as a rule, absent, though when present they are usually in the form of pointed threads or splinters.

The *life-history* of *E. coli* is similar to that of *E. histolytica*, save that the large vegetative forms inhabit the fæces, instead of the tissues of their host

Digitized by Google

as in the latter species. In spite of many attempts and claims to the contrary, neither *E. coli* nor *E. histolytica* has yet been cultivated upon artificial media. It is probable that the organisms which have been described in the hitherto recorded successful attempts have been free-living species of amœbæ. *E. coli* is not affected by emetine.

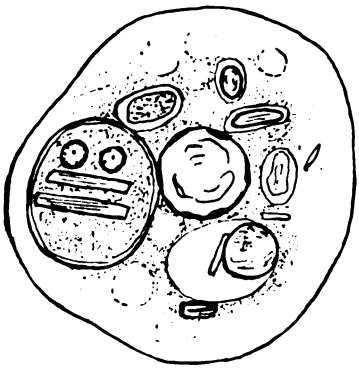


Fig. 237.—Entamœba coli with ingested binuclear E. histolytica cyst. × 2,000 diameters. (*After Wenyon and O'Connor.*)

Incidence of E. coli.—This organism is common in man, both in temperate zones and in the tropics. Dealing with large numbers of examinations in diarrhœic and dysenteric conditions in British and Egyptian troops, O'Connor found it in 25 per cent., and, together with Wenyon, this observer recorded *E. coli* cysts in almost the same proportion of healthy troops. About 15 per cent. of *coli* infections have been reported among normal army recruits in England.

Entamœba gingivalis (Gros, 1849; Brumpt, 1913 (Fig. 238).—The amœba of the mouth was the first amœba discovered in man, and was considered by Bass and Johns (1915) to be the cause of pyorrhœa alveolaris, but this has to a great extent been disproved. It is a small amœba showing great variations in size—from 10 μ to 25 μ in diameter, according to Dobell. Endoplasm and ectoplasm are rather sharply differentiated, and the cytoplasm is filled with food vacuoles and peculiar inclusions of a greenish, refractile appearance. The nucleus is spherical and

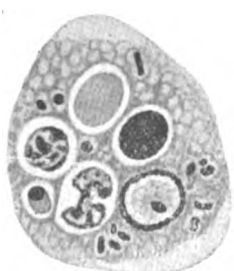


Fig. 238.—Entamœba gingivalis: active amœboid form with excentric nucleus and ingested bodies. × 2,500 diam. (*After Dobell.*)

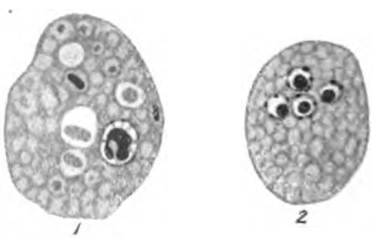


Fig. 239.—Endolimax nana. × 2,500 diam. (*After Dobell.*)

1, Active amæboid form; 2, quadrinucleate mature cyst.

vesicular, in diameter from 2·5 μ to 3 μ, and is slightly smaller in proportion to the rest of the organism than is the nucleus of *E. histolytica* or *E. coli*. The nuclear membrane is very definite. The karyosome itself consists entirely of chromatin. Apart from the peculiar bodies, which may be the

Digitized by Google

remains of salivary corpuscles or polymorphonuclear cells, *E. gingivalis* usually contains large numbers of bacteria. The amœba probably reproduces by binary fission, although all the stages have not been observed. It is also probable that this species does not form cysts, though bodies believed to constitute this stage have been described. The claim of *E. gingivalis* to pathogenicity is more than doubtful.

Endolimax nana (Wenyon and O'Connor, 1917), Brug, 1918 (Fig. 239), is of importance in so far that its quadrinucleate cysts resemble the smaller cysts of *Entamœba histolytica*. It is commonly present in normal fæces, and has been recorded in some 33 per cent. of dysenteric and diarrhœic stools. It is a small amœba, 6–12 μ in diameter, with characteristic vesicular nucleus and a large and irregularly shaped *excentric* karyosome. It probably inhabits the small intestine and lives upon the intestinal contents. The *cysts* (Fig. 239, 2) are oval, characteristic structures of the same size as the vegetative form, and contain, when mature, four nuclei, a few visible refractile granules, but no vacuoles or chromatoid bodies. Glycogen cannot always be demonstrated in the cysts; it is most commonly found in the binucleate forms. The cysts vary in shape from a typical oval to a sphere; very small ones are 6 μ in diameter. Occasionally they contain peculiar inclusions resembling long and filamentous rods or granules, and are then liable to be mistaken for cysts of *Giardia intestinalis*.

Like *Entamœba coli*, *Endolimax nana* is non-pathogenic and is not amenable to emetine treatment.

TABLE SHOWING DIFFERENTIAL CHARACTERS OF THE COMMONER INTESTINAL AMŒBÆ

Entamœba coli	*Entamœba histolytica*	*Endolimax nana*
Size: 18–40 μ.	18–40 μ.	6–12 μ.
Morphology: No distinction between endo- and ectoplasm.	Granular endoplasm; clear ectoplasm.	Granular and rather vacuolated cytoplasm.
Contains much ingested food material.	Ingests red cells, tissue cells, etc.	Ingests bacteria and food granules.
Nucleus large and distinctive, nuclear ring, and excentric karyosome.	Nucleus inconspicuous in fresh specimens. Smaller size, beaded nuclear ring, central karyosome.	Well-marked nuclear membrane and excentric massive karyosome.
Sluggish movement.	Active blunt pseudopodia.	Sluggish movement.
Multiplication: In fæces by binary fission. Encystment and formation of 1, 2, 4, and 8 nucleated round cysts, 10–30 μ in diameter.	By fission in *intestinal wall*. On fæces becoming hard, encystment and formation of quadrinucleate cysts, 7–15 μ in diameter.	In fæces by binary fission; formation of oval cysts 8 10 μ in length by 7–8 μ in breadth.
Chromatoid bodies typically not present in the mature cyst.	Commonly containing chromatoid bodies.	Uninucleate, binucleate, and quadrinucleate cysts, contain no chromatoid granules.

Iodamœba bütschlii (Prowazek, 1912), Dobell, 1919 (Fig. 240).—The cysts formerly described as "iodine" or "I. cysts" in human fæces are now definitely known to belong to this species. It is a small amœba, intermediate

Digitized by Google

in size between *E. coli* and *E. nana*, measuring from 9–20 μ in diameter, though very small individuals 5 μ in size have been recognized. In form and habit it is very like a small specimen of *E. coli*. The cytoplasm is filled with food vacuoles containing bacteria and other food particles. The nucleus is often quite invisible in organisms containing much food. It is vesicular, with a moderate-sized central, intensely-staining karyosome, 2–3·5 μ, about one-fourth to one-fifth the size of the whole organism. The nuclear membrane is well developed. Between it and the karyosome is a clear zone occupied by a layer of small granules. *I. bütschlii* feeds chiefly upon the micro-organisms of the large intestine which it inhabits. The usual method of multiplication of this amœba seems to be by simple bipartition.

The *cysts* are remarkable uninucleated structures, very frequently irregular in outline, it may be spherical or oval, and measure 9–12 μ in diameter. Owing to the irregularities in their shape, they are often difficult to measure with certainty, but 6–16 μ may be taken as extremes. They contain numerous refractile volutin granules and, almost invariably, a comparatively large

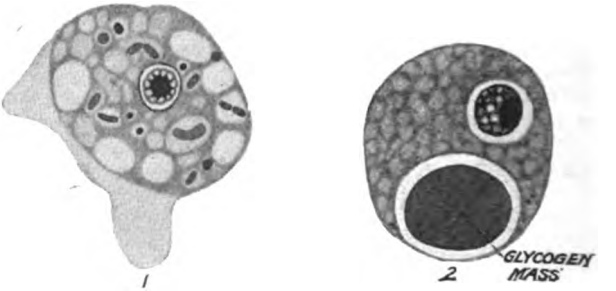


Fig. 240.—Iodamœba bütschlii. × 2,500 diam. (*After Dobell.*)

1, Active amœboid form with ingested micro-organisms ; 2, mature cyst, "iodine cyst," containing large glycogen mass.

and dense glycogen mass, most readily studied when the cysts are suspended in iodine solution. Sometimes two or even three separate masses may be found in the same cyst. The cyst nucleus, excentrically placed, is of a comparatively large size, 2–2·5 μ. The karyosome, which is centrally situated in the active precystic amœba, gradually passes to the periphery and becomes a large compact mass in contact with the nuclear membrane in the cyst.

The mature uninucleate cysts of this amœba, save for the disappearance of the contained glycogen, undergo no further changes outside the human body.

I. bütschlii occurs in about 5 per cent. of fæces, and most commonly in those who have been in the tropics, and usually in association with *E. histolytica*.

Both the vegetative forms of *I. bütschlii* and its cysts are extremely amenable to emetine and emetine-bismuthous-iodide. Precisely how this is effected it is difficult to say, for if emetine be an amœbicide, as was thought to be the case, it is strange that it is without effect upon *E. coli* and *E. nana*.

Dientamœba fragilis, Jepps and Dobell, 1918 (Fig. 241), is a very small amœba, 3·5–12 μ in diameter, its usual size being 8–9 μ. It lives in the large

Digitized by Google

intestine. It is actively motile, with marked differentiation between ecto- and endoplasm. The pseudopodia are lobed and indented. It is a very rare amœba, and only very few cases have so far been described. Each individual is typically binucleate. In size the nucleus ranges from 0·8 μ to 2·3 μ; this structure is spherical and vesicular, the karyosome being large and composed of a number of granules embedded in a plastin matrix. After leaving the body the amœba quickly degenerates. No cysts have, as yet, been found. It would appear to live exclusively upon bacteria and other small micro-organisms.

"**Amœba limax**" is a term applied to many different free-living forms of amœba occurring in water and earth. The cysts possess a hard and

Fig. 241.—Dientamœba fragilis, uninucleate and binucleate forms. × 2,500 diam. (*After Dobell.*)

refractile wall. These forms are of importance to the tropical pathologist in that they may be ingested and recovered from the stools of dysenterics and normal individuals by culture on Musgrave and Clegg's medium.

Class II.—MASTIGOPHORA

The Mastigophora are divided into several subclasses, of which only one, that of the *Flagellata*, demands our attention, and within this group we shall consider only the two orders Protomonadina and Polymastigina.

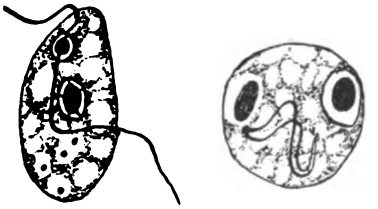


Fig. 242.—Prowazekia cruzi. × 2,000 diam. (*After Brumpt.*)

Order I.—PROTOMONADINA

The Protomonadina are mostly flagellates of a small size with one or two flagella. They may be parasitic, commensal, or free-living.

Bodo (= Prowazekia).—Flagellates belonging to this genus are found in decomposing urine or fæces kept outside the body. They have a rough resemblance to *Trypanoplasma* in possessing a kinetonucleus and two flagella. Several species have been described, but their differentiation is by no means easy. They have few if any claims to pathogenicity. The species from urine and fæces are easily cultivated and form characteristic cysts. (Fig. 242.)

The **Hæmoflagellata** and allied forms are an important suborder of the

Digitized by Google

Protomonadina, and under this term are grouped a number of forms having a characteristic, but not invariably parasitic, habitat in the blood of vertebrates and in the digestive tract of invertebrates.

The group comprises a number of heterogeneous forms conveniently grouped together, their chief morphological feature being the possession of two nuclei—a *tropho-* and a *kinetonucleus*.

The genera representing the more important types are—(1) Trypanosoma, (2) Trypanoplasma, (3) Crithidia, (4) Herpetomonas, (5) Leishmania.

1. The Genus Trypanosoma

The structure of the trypanosome body is of a uniform type, though subject to variation in minor details. The body is long and sinuous; the anterior * end tapers gradually to a fine point, while the posterior end generally terminates more bluntly. (Fig. 243.)

The principal nucleus (trophonucleus) is situated centrally; the kinetonucleus is usually placed posteriorly to the nucleus, but is sometimes closely approximated to it. Certain exceptions to this rule are known, namely, *T. rhodesiense* (p. 135) and some multiplicative forms of *T. lewisi*. The flagellum arises from a blepharoplast, or basal granule, closely connected

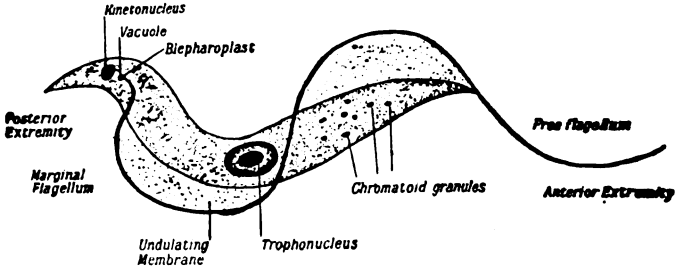


Fig. 243.—Schema of trypanosoma. (*After Dobell.*)

with the kinetonucleus, and passes forwards as the margin of the undulating membrane; in some cases it may end with the undulating membrane at the anterior extremity of the body, but more usually it projects forwards as a free lash. In one species, *T. equinum* (Fig. 246, *a*), the cause of "mal de caderas," the kinetonucleus is very minute.

Trypanosomes occur as blood parasites in all classes of vertebrates. Many wild animals harbour small numbers of them in their blood. Certain are specific but probably harmless to their particular vertebrate host.

Trypanosomes of cold-blooded animals include *T. granulosum* and *T. rotatorium* (Figs. 244 and 245).

Though showing but slight morphological differences as a general rule, members of this genus have been differentiated on morphological as well as on pathological grounds.

The trypanosomes of birds probably develop in mosquitoes; those of fishes and turtles in leeches.

* The terms "flagellar" and "aflagellar" may be used to designate the extremities of the body, instead of the terms "anterior" and "posterior" respectively, which are here employed strictly with reference to the mode of progression.

Digitized by Google

Two methods of transmission of trypanosomes must be distinguished. The one, a mechanical method, can be performed by any blood-sucking insect for a few hours after a meal of infected blood; the other, indirect or cyclical, involves a developmental cycle, and can only take place in the particular intermediate host to which that species of trypanosome has become adapted.

The development of *T. gambiense* (Fig. 243) in the tse-tse fly, *Glossina palpalis*, thanks to the researches of Bruce and his collaborators, Kleine, Taute, and Miss Muriel Robertson, is now fairly completely known. Apparently development takes eighteen to twenty-five days or longer to complete. Five to seven days after ingestion of infected blood the trypanosomes become scarce in the digestive tract of the fly, only to reappear in large numbers and in a variety of crithidial and other forms. Finally, an invasion of the salivary glands by short, stumpy, trypaniform individuals takes place. In *T. vivax* (*cazalboui*) a completely different mode of development in Glossina takes place, a method termed by Roubaud *évolution par fixation directe*; this occurs solely in the proboscis of *Glossina palpalis*. The trypanosomes assume a different shape and attach themselves by their flagella to the labium or hypopharynx of the proboscis tube, multiplying in the salivary

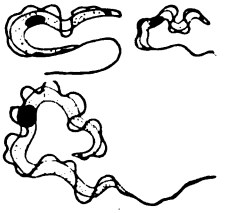


Fig. 244.—T. granulosum. A trypanosome of the eel.

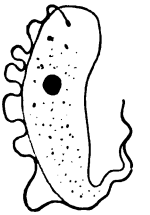


Fig. 245.—T. rotatorium. (*After Laveran.*) A trypanosome of the frog (Rana esculenta).

fluid; flies in this condition remain infective for life. A third mode of development occurs in the case of *T. dimorphon*—the *évolution par fixation indirecte* of Roubaud. In this case the trypanosomes multiply first in the digestive tract of the Glossina, and then pass forwards into the proboscis.

In *T. cruzi* the development, both in the intermediary and in the definitive host, is of so different a character that Chagas has relegated it to a special genus, *Schizotrypanum*. In man the adult trypanosomes multiply, not in the peripheral circulation, but in the internal organs of the body. In the capillaries of the lungs the adult trypanosome loses its flagellum, the body becomes round, and the mass breaks up into eight small individuals (merozoites). A second type, and probably the normal method of multiplication in man, takes place within the hypertrophied endothelial cells of the lung and striped muscles, notably the cardiac muscle, but can apparently occur in any tissue. In this situation the parasite assumes the shape and appearance of a *Leishmania*. The developmental cycle of this trypanosome takes place in a bug, *Conorhinus megistus*, and is shortly as follows: The trypanosomes taken up into the bug's stomach change in about six hours. Having lost their flagella, they assume a leishmania form and multiply by fission. After a time these forms acquire a crithidial shape and pass into the intestine, eventually gaining the body cavity and salivary

Digitized by Google

glands of the insect as small trypanosomes, and in this form are transmitted to the vertebrate host.

BRUCE'S CLASSIFICATION OF PATHOGENIC AFRICAN TRYPANOSOMES

	FORM	CYTOPLASM	KINETONUCLEUS	UNDULATING MEMBRANE	MOVEMENT	DEVELOPMENT IN TSE-TSE	SUSCEPTIBLE ANIMALS
A. *Trypanosoma brucei* Group, including *T. brucei*—*T. gambiense* *T. rhodesiense* *T. evansi*	Polymorphic, including short and stumpy forms	Contain dark-staining granules	Small and coarse, at some distance from posterior end	Well developed and in bold folds	Active	Completed in salivary glands	Many species of mammals
B. *Trypanosoma pecorum* Group, including *T. pecorum* *T. simiæ*	Monomorphic and small	Non-granular	Prominent and subterminal	Well developed	Active	Completed in proboscis and hypopharynx. Never found in salivary glands	Cattle—very fatal to pigs
C. *Trypanosoma vivax* Group, including *T. vivax* *T. caprae* *T. uniforme*	Monomorphic	Non-granular	Large and terminal	Little development and simple	Very rapid	Completed in proboscis and hypopharynx. Never found in salivary glands	Affects only horses, cattle, goats, and sheep. Ordinary laboratory animals immune

The changes undergone by trypanosomes in culture on N.N.N. medium (p. 894) are diverse and striking: therein they exhibit a series of forms quite distinct from those seen in the blood of the vertebrate, and bearing more

Digitized by Google

resemblance to those seen in the invertebrate host. In such cultures they assumec rithidial, leptomonal, and even leishmanial forms.

Though filtrations of infected blood plasma through a bacterial filter have been experimented with, there has been no confirmation of Schaudinn's statement to the effect that some part of the development of trypanosomes in the blood is ultramicroscopic.

In some instances trypanosomes appear in the peripheral circulation only at certain periods, as in the case of *T. rhodesiense* in man; and in others, as in the trypanosome of *Athene noctua*—the little owl—they are said to be most numerous in the peripheral circulation during the night-time throughout the summer months; in the winter months they are found in the bone-marrow.

Trypanosoma gambiense, Dutton, 1902, possesses a characteristic trypaniform shape. It varies much in length and breadth during different stages of its existence; as a general rule it measures 18–30 μ in length by 1–3 μ in breadth. The young and recently divided forms have a short flagellum, and the blepharoplast is terminally situated. The organism is more numerous in human blood, though it multiplies rapidly when injected into laboratory animals, especially rats and monkeys. The life-history of *T. gambiense* has already been fully described (p. 120), but it may be added that certain short forms (13–20 μ in length) occurring in the blood represent the adult forms, and that when taken up by *Glossina palpalis* they multiply in the hindgut, and trypanosomes of very varying sizes result. From the tenth to the fifteenth day after ingestion, long slender forms, the so-called "proventricular types," move forwards into the proventriculus. After becoming well established they pass into the hypopharynx and along the salivary ducts into the salivary glands. The fly never becomes infective till this happens, usually from the twentieth to the thirtieth day.

The reed buck and other antelopes are considered to be the natural reservoirs of this trypanosome. *T. nigeriense* is considered by some to be merely a variety of this species.

T. rhodesiense, Stephens and Fantham, 1910, resembles *T. gambiense* in its general morphological characters, but possesses more virulent pathogenic properties, is very resistant to treatment, and is restricted to Southern Nyasaland, North-Eastern Rhodesia, and Portuguese East Africa, but is apparently extending its range. When injected into experimental animals it assumes a posterior-nucleated form about the fifth or sixth day after injection. Kinghorn and Yorke, in 1912, demonstrated the transmission of *T. rhodesiense* by *Glossina morsitans*, about 5 per cent. of which became infected. It is a very virulent infection to monkeys, and was thought to be identical with *T. brucei*, but recent experiments by Taute have shown that this is probably not the case.

T. lewisi (Kent, 1879) is a parasite of rats (*R. decumanus*, *R. rattus*, *R. rufescens*). Similar parasites in hamsters, guinea-pigs, rabbits, etc., probably belong to different species; it has been held that *T. lewisi* is not capable of living in these animals, but subsequent work seems to contradict this. These subspecies have been named *T. cuniculi*, *T. microti*, and *T. duttoni*.

On account of the facility with which it can be procured in most countries, *T. lewisi* offers the best opportunity for study of the genus. In many places from 2 to 50 per cent. of the local rats harbour it, often in such abundance that, viewed through the microscope, the blood seems to seethe and quiver with the rapidly moving parasites. Specimens are easily procured by snipping

Digitized by Google

off with scissors the tip of the rat's tail and dabbing the cut surface on the slip.

T. lewisi measures, on an average, including the flagellum, 24–25 μ by 1·5 μ; the posterior extremity is said to be more pointed than in the other known mammalian trypanosomes. The nucleus is situated in the anterior half or third of the body; the cytoplasm is very clear and free from granules. There is evidence that it is conveyed from rat to rat by the rat-louse and rat-fleas, *Hæmatopinus spinulosus*, *Ceratophyllus fasciatus*, and *Xenopsylla cheopis*, which are now known to be its true intermediary hosts. Apparently it is not transmitted via the salivary glands of the insect, but multiplies in the hindgut of the flea and, after assuming various crithidial forms, escapes in the excreta, and is thus inoculated into the wound made by the flea's proboscis.

In experimental rats it has been found possible to transmit the infection to other rats through the unbroken skin by rubbing on cultures of the trypanosome.

It is generally held that *T. lewisi* is non-pathogenic. Certainly, infected rats usually exhibit a remarkable tolerance towards this parasite, but occasionally they do sicken and die.

The fact that the rat is susceptible to laboratory inoculation with the

Fig. 246.—Trypanosomes of mammals. × 1,000.

a, T. equinum; *b*, T. brucei; *c*, T. equiperdum; *d*, T. lewisi; *e*, T. evansi.

trypanosomes of man and cattle indicates the possibility of finding other species of trypanosomes in the blood of wild rats.

T. evansi (Steel, 1885); length, 22–30 μ; breadth, 1–2·5 μ. This parasite was discovered in 1880 by Griffith Evans in the Punjab, in the blood of horses suffering from surra, a disease which the natives of India ascribe to the bite of certain horse-flies (*Tabanidæ*). *T. evansi* is not limited to horses and mules, but infects also camels, elephants, buffaloes, and dogs. Experimentally it has been transmitted to monkeys, rabbits, rats, mice, and guinea-pigs; in nature, infection of dogs by feeding on animals dead of surra has frequently been observed. It has a very wide distribution in Southern Asia and in Malaya, and has been recently imported into Mauritius and the Philippines. We have no positive knowledge as to the definitive host or hosts of this trypanosome. Various blood-sucking flies which belong to the genera *Stomoxys*, *Hæmatobia*, and *Tabanus* have been suspected. In Mauritius the epidemic is thought to have been spread by *Stomoxys nigra*.

In South America a similar disease occurs in mules and is known as "murrina"; the parasite has been considered a subspecies, *T. hippicum*.

The disease known as "mbori," occurring among dromedaries coming from the Sahara into the Sudan (Timbuctoo, etc.), which is apparently also conveyed by a tabanus, *T. ditæniatus*, is considered both by Vallée and

Digitized by Google

Panisset and by Laveran and Mesnil to be a milder form of surra; the parasite which causes it being a "variety" of *T. evansi*, known as *T. somaliense*.

T. brucei (*T. pecaudi*) (Plimmer and Bradford, 1899); length, 28–30 μ; breadth, 1·5–2·5 μ. The anterior extremity is usually bluntly rounded. The cytoplasm often contains in the posterior half large, deeply staining granules. This parasite was discovered by Bruce in 1895 in the blood of horses suffering from nagana, the "fly disease" of Africa. The normal intermediary hosts of *T. brucei* are probably some of the African *Antelopidæ*, such as the wildebeest (*Catoblepas gnu*), the koodoo (*Strepsiceros capensis*), and the bushbuck (*Tragelaphus scriptus sylvaticus*), perhaps also buffaloes. Bruce's researches and experiments led to the belief that the disease was transmitted in a mechanical way by *Glossina morsitans*, but it is now known to take place through the salivary glands. Austen has shown that the tse-tse flies with which Bruce made his experiments belonged chiefly, if not entirely, to the species *G. pallidipes*; and now we know that other glossinæ, such as *G. fusca* and *G. brevipalpis*, may also convey the disease, and that the rôle played by these flies is probably that of true intermediary host. The development in the fly is identical with that described for *gambiense*. The fly does not become infective till the eighteenth, and remains so till the sixty-sixth day—probably longer, after feeding upon an infected monkey.

With the exception of certain strains of donkey and goat, all domesticated mammals hitherto experimented with, on inoculation with blood containing the parasite, acquire nagana.

After inoculation of an animal with nagana blood, in from one to two days trypanosomes begin to appear in the blood, and persist therein till death, which, in the vast majority of species, is inevitable. In some species (rats and mice) the trypanosomes become very numerous; in others (rabbit, guinea-pig) they are scanty and may be hard to find with the microscope, although their presence may readily be proved by the symptoms and by injection of the suspected blood into the rat. After inoculation death occurs in rats and mice in from 2 to 3 days, in rabbits in from 5 to 12 days, in guinea-pigs in about 50 days (extremes 20 to 183 days), in dogs in from 22 to 26 days, in monkeys in 15 days, in horses and donkeys in from 1 week to 3 months, in goats and sheep in several months; and in cattle in from 1 week to 6 months, a proportion recovering. Thus resistance varies within wide limits.

In those animals in which death occurs within a few days of infection the parasites become very numerous, and, after one or two oscillations of temperature, death occurs suddenly. In those animals in which death is delayed a very striking cachexia is established. There is a chronic recurring fever, the numbers of parasites visible in the blood being greatest during the febrile accessions. There is also a peculiar firm œdema from infiltration of coagulable lymph into the connective tissue of the neck, abdomen, sheath of penis, genitals, and limbs; together with intense anæmia, wasting, skin eruptions and, often, blindness. On post-mortem examination the spleen is in most instances found to be enlarged, ecchymoses may be present in various viscera, and the lymphatic glands corresponding to the point of inoculation are swollen.

Other trypanosomes, more or less allied to *T. brucei*, and possibly representing only varieties of the same parasite, have been observed in German East Africa and Togoland in cattle, horses, and other animals. Again, the disease known as "aino," which occurs in Somaliland among dromedaries,

Digitized by Google

and which Brumpt believes to be transmitted by *G. longipennis*, is probably a form of nagana.

T. equiperdum (*T. rougeti*) (Dofl., 1901); length, 25–28 μ; breadth, 1·5–2 μ; differs from *T. brucei* in not having prominent granules in the cytoplasm. It is the cause of a peculiar disease in stallions, brood mares, and donkeys, occurring in South Europe, North Africa, Chile, and probably in the United States, and known as "dourine" or "mal du coït." The latter name it has received from the fact that, as a rule, the infection is communicated through coitus. It is not yet certain whether the parasites have any alternate insect host into which they must pass at intervals in order to complete the life-cycle. Fleas have been suggested as possible intermediaries.

Symptoms appear in from ten to twenty days after infection. They begin in the case of the stallion with œdema of the sheath, some inflammation of the end of the penis, and discharge from the urethra; in the mare there is a similar œdema of one or both labia and a muco-purulent vaginitis. Concurrently with increase of these symptoms œdema of the limbs and of the abdominal walls sets in, together with progressive anæmia, wasting, muscular weakness, flexion of the fetlocks, and skin eruptions. The appetite is preserved. Fever, except at the outset (40° C.), rarely exceeds 39° C. The disease continues for many months—four to ten. Before death weakness increases, the cornea may ulcerate, and there may be complete paraplegia from softening of the spinal cord.

The trypanosome of dourine occurs in the blood, but in numbers so scanty that to communicate the infection with certainty by this medium it may be necessary to inject from 10 to 15 c.c. Hence the improbability of infection being transmitted by biting insects. On the other hand, it occurs in great abundance in the œdematous tissues, in the skin lesions, in the lymph, and in the discharge from the genitals.

In marked contrast with *T. brucei*, *T. equiperdum* is but feebly pathogenic to rats and mice, some of the former being quite refractory. In the rabbit and dog the disease resembles that in the horse, and is communicable by coitus. Monkeys, goats, sheep, and bovines are said to be insusceptible.

Although in many respects the parasites of dourine and nagana resemble each other, the differences in susceptibility of various animals as regards the two parasites indicate specific difference.

T. equinum (Voges, 1902); length, 22–55 μ; breadth, 1·5–2 μ.—This parasite is clearly distinguished from the above-mentioned species by the very minute size of its blepharoplast. The cytoplasm contains granules, but not so numerous as in *T. brucei*. Its normal vertebrate host is probably the capybara, *Hydrochœrus capybara*, a large water mammal of South America, belonging to the family *Caviidæ*. Nothing positive is known about its transmitting agent; *Stomoxys calcitrans* and *Stomoxys nebulosa* have been blamed. *T. equinum* causes in horses a deadly disease known as "mal de caderas" in Brazil, Argentina, and Central South America.

T. theileri, Laveran, 1902.—Theiler discovered in the Transvaal a trypanosome twice the size (60–70 μ in length by 5 μ in breadth) of any of the foregoing, and peculiar to cattle; so far, other domestic animals have been found to be immune. It is now regarded as being non-pathogenic. Theiler believed that the transmitter of this parasite was a spider-fly, *Hippobosca rufipes*. Another species of fly, *H. maculata*, recently imported with cavalry from India, is believed to be aiding in spreading the parasite. A variety known as *T. ingens*, found in cattle in Uganda, is still larger than *T. theileri*, and measures 72–122 μ in length, the flagellum alone measuring 17 μ.

Digitized by Google

T. pecaudi, Laveran, 1907.—This parasite, first recorded from Northern Nigeria in horses and donkeys, causes a disease termed "baleri." It is now known to extend to Senegal, Ivory Coast, Dahomey, French Congo, and possibly the Bahr-el-Ghazal. Cattle are also susceptible. It is a very active trypanosome, of which two forms, a long thin and a broad short one, may be distinguished. The former measures 25–35 μ in length by 1·5 μ in breadth; the undulating membrane is very narrow and the flagellum is free anteriorly for about one-quarter its length; the cytoplasm contains no granules. The short form measures 14–20 μ in length by 3–4 μ in breadth; the undulating membrane is well developed and there is no free flagellum; the cytoplasm may be very granular.

T. pecaudi is transmitted mainly by *Glossina longipalpis*, though *G. tachinoides*, *G. palpalis*, and *G. morsitans* may also subserve. The incubation period in the intestinal canal of the insect is twenty-three days; development is completed in the proboscis and hypopharynx.

T. vivax, Ziemann, 1905, is probably synonymous with *T. cazalboui*; it is a parasite of cattle, sheep, and goats on the Upper Niger and in the Cameroons, Congo Free State, Uganda, and Rhodesia. The disease it produces in these animals is known as "souma." Horses, mules, and donkeys are affected in a lesser degree, but dogs, cats, monkeys, pigs, rats, and mice are refractory; this differentiates the parasite from allied forms. It is a monomorphic species and is very active; in many ways it is related to *T. uniforme*. Individual trypanosomes measure 24 μ in length by 1·5 to 2 μ in breadth. The posterior extremity is rounded, the nucleus is oval, the kinetonucleus being situated posteriorly. The undulating membrane does not exhibit any marked folding as in *T. lewisi*; the flagellum is free posteriorly.

Development takes place in various glossinæ, *G. palpalis*, *G. tachinoides*, *G. longipalpis*, and *G. morsitans*, especially the first-named species, and is confined to the proboscis; the insects become infective after a period of from six to seven days. In the proboscis the trypanosomes rapidly change into leptomonal and crithidial forms, and attach themselves to the walls of the labrum, resulting in the production of clusters of flagellates which, under the influence of the salivary secretion, develop into small, actively motile trypanosomes.

A variety of this species, named *T. capræ*, has been described by Kleine from goats in Tanganyika.

T. uniforme, Bruce and Hamerton, 1911, is a parasite of cattle in Uganda. Goats and sheep are relatively refractory. It occurs as a natural infection in the bushbuck and sitatunga (*Tragelaphus spekei*). Monkeys, pigs, dogs, cats, and rats are relatively refractory, in which respect it resembles *T. vivax*. It is a small, active trypanosome, remarkably uniform in size and appearance, measuring 16 μ in length by 1·5–2·5 μ in breadth. The free portion of the flagellum is from 1 to 5 μ in length. It is transmitted by *Glossina palpalis*, and development proceeds within the proboscis, as in *T. vivax*. Apparently this parasite has not very pronounced pathogenic properties, for it may persist for years without producing any symptoms.

T. dimorphon, Laveran and Mesnil, 1904, is widely distributed throughout West Africa, and is a parasite of horses, mules, cattle, sheep, and pigs, while dogs, cats, and most laboratory animals are susceptible. Its pathogenicity is not of a high order. As its name implies, it is a most dimorphic species. The long forms are rare, and measure 20–25 μ in length by 1·5 μ in breadth; the short forms are much the more frequent, measuring 12–14 μ in length by 1 μ in breadth; the posterior extremity is rounded and the

Digitized by Google

undulating membrane only slightly developed. Between these two forms are many intermediate ones. In stained specimens the protoplasm takes on an intensely blue colour. Development takes place in *Glossina palpalis*, *G. morsitans*, *G. tachinoides*, and *G. longipalpis* by the process known as *évolution par fixation indirecte*; that is to say, after becoming established in the hind-gut, the parasites gradually extend to the proboscis, where they multiply into leptomonal and crithidial forms.

T. pecorum, Bruce and Hamerton, 1910, is a parasite of horses and cattle in Uganda, and is chiefly related to *T. dimorphon*. It is also found in the blood of the big game in N.E. Rhodesia. The disease has an incubation period of six to seven days, and is invariably fatal within a year. The parasite is a monomorphic species; the average individual measurements are 14 μ in length by 3 μ in breadth. Posteriorly it is rounded, anteriorly it is tapering, and the undulating membrane is well developed but presents no free flagellum. The oval nucleus is situated in the centre of the body, and the spherical kinetonucleus at the posterior end. In fresh preparations the parasite exhibits alternate periods of quiescence and activity; in the former state it is difficult to detect, as it is usually buried under clumps of red cells. The usual intermediary hosts are *Glossina morsitans*, and under experimental conditions *G. palpalis* as well. The development, as in the case of *T. dimorphon*, is indirect and is completed within the proboscis; in *Glossina palpalis* the process is extremely slow, and is not complete till the seventy-sixth day after ingestion.

T. nanum, Laveran, 1905, and **T. congolese**, Broden, 1904, are morphologically indistinguishable from *T. pecorum*, but on account of cross-immunity reactions have been separated by Laveran and Mesnil. The former parasite is found in cattle in the Sudan and East Africa; the latter in those animals, as well as in donkeys, sheep, and other domestic animals, in the Congo Free State and North-East Rhodesia. Development takes place in *Glossina palpalis*, and is similar to that described for *T. pecorum*.

T. simiæ, Bruce, Harvey Hamerton, 1912, has been recorded from Nyasaland and North-East Rhodesia, and affects monkeys and goats. Oxen, dogs, and other laboratory animals appear to be immune. In the former animals the disease runs a rapid and fatal course. It is a very active parasite when seen under the microscope, and measures 14–24 μ in length by 1–2·75 μ in breadth. It is monomorphic, uniform in shape, and occurs in large numbers. It is transmitted by *Glossina morsitans*, but details of its development in that insect have not yet been worked out.

T. (Schizotrypanum) cruzi, Chagas, was discovered in man by Chagas, in 1909, in Rio de Janeiro. When present in the bloodstream it very much resembles *T. gambiense*, and produces a peculiar form of trypanosomiasis in Brazil (p. 138). In the peripheral blood these parasites measure 20 μ in length. Certain individuals leave the bloodstream, enter the musculature, especially the heart or brain tissue, and there undergo schizogony and become transformed into leishmania-like forms, which in about five days reproduce other characteristic protozoa. The sexual forms are ingested by a Reduviid bug, *Conorhinus megistus*, and undergo an elaborate development in its body, as has already been described (p. 140).

2. The Genus Trypanoplasma (Fig. 247)

The species of this genus parasitic in blood are only known as yet to occur in fresh-water fishes, and are transmitted by leeches. A number of species are parasitic in the organs of snails, such as *T. helicis*, found in the receptacu-

Digitized by Google

lum seminis of *Helix pomatia*. The principal feature is the presence of two flagella arising together from two blepharoplasts at the anterior extremity. There is a large kinetonucleus. One flagellum projects forwards, the other passes down the side of the body to the hind end, forming the free edge of the undulating membrane and projecting backwards as a free flagellum.

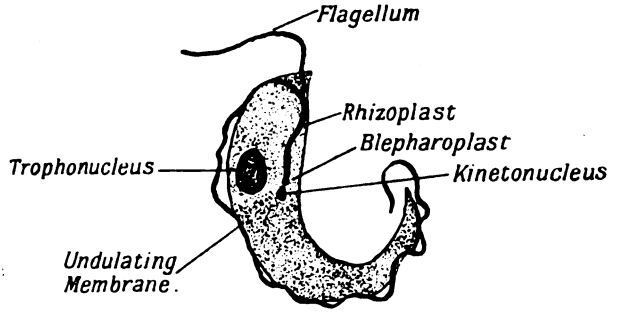


Fig. 247.—Trypanoplasma. × 2,000 diam. (*After Brumpt.*)

3. The Genus Crithidia (Fig. 248, B)

The distinctive feature of this genus is the relatively short undulating membrane and flagellum arising from the centre of the body at a point in close proximity to the kinetonucleus. The shape of the body varies considerably. Crithidial stages are commonly found as developmental forms of trypanosomes. There remain, however, a number of forms which are parasitic in the intestinal tract of insects, notably the Chironomidæ and Pulicidæ.

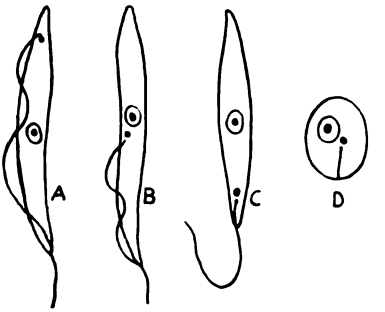


Fig. 248.—Diagram of types of flagellates. (*After Wenyon.*)
A, Trypanosome; B, Crithidia; C, Leptomonas; D, Leishmania.

4. The Genus Herpetomonas (or Leptomonas)

These are intestinal parasites of insects, especially the Muscidæ and the Hemiptera. In most cases they are parasites of insects alone, infection being brought about by the ingestion of cyst-infected fæces. Some species are parasitic in the latex of plants, and are taken up by the appropriate plant hemiptera. The distinctive characters (Fig. 248, C) are the possession of a

Digitized by Google

single flagellum arising from a single blepharoplast situated in the anterior portion of the body, and the absence of an undulating membrane. Uniflagellate and biflagellate forms occur. Some authorities regard the latter as the result of precocious formation of a new flagellum in anticipation of longitudinal division. They have shown that forms resembling trypanosomes also occur, the changes in form being, in all probability, brought about by the migration of the nuclei; all stages being found between the non-flagellate leishmania, through leptomonal, crithidial, to the trypanosome form (Fig. 248).

5. The Genus Leishmania

This genus includes human parasites, *L. donovani* (Fig. 249), the cause of a general disease, kala-azar, and *L. tropica*, the cause of oriental sore. *L. donovani* (= *infantum*), in the Mediterranean area, is found especially in children, and is associated with a similar disease occurring in dogs and caused by the same parasite. The type of parasite found in the vertebrate host is a small oval body multiplying by fission and contained within cells—endothelial cells or macrophages; it is very uniform in size. Each parasite possesses a tropho- and a very distinct kinetonucleus.

In cultures on the N.N.N. medium the leishmanias increase in size and develop a flagellum, finally assuming an elongated leptomonas form. It is

Fig. 249.—Leishmania donovani. (*After Leishman.*)

thought that this latter represents a stage of the development of the parasite in the invertebrate host; such a development, however, has not yet been worked out. Patton believed that in the case of *L. donovani* the parasite completes its development cycle in *Cimex hemipterus* (*rotundatus*), and in the Mediterranean area there is a certain amount of evidence tending to incriminate *Ctenocephalus canis*, the dog-flea, as being the definitive host. In the case of *L. tropica*, it has been pointed out that since the sores, as they occur in man, are situated on some uncovered part of the body, the invertebrate host is more likely to be some biting fly or mosquito, or even the sandfly (*Phlebotomus*).

Nomenclature of the hæmoflagellates.—The generic terms given to these different parasites are also utilized to denote the different stages in their life-cycles. Of this cycle the leishmania is taken to represent the most primitive, the trypanosome of vertebrates the most highly developed form (Fig. 250).

All stages in the developmental forms of certain trypanosomes occur in cultures, just as they do in the gut of the definitive host—the glossina, and even in the vertebrate host, as in *T. lewisi*. The generic titles *Trypanosoma*, *Herpetomonas*, *Crithidia*, and *Leptomonas* should, strictly speaking, be reserved for the parasite according to the highest developmental form it is capable of assuming. The accompanying diagrams, taken from Wenyon (Figs. 248, 250), illustrate this idea.

Digitized by Google

Parasites of Uncertain Zoological Position resembling Leishmania

Hæmocystozoon braziliense was found by Franchini in the blood of a man from Brazil. The parasites are sometimes oval, the size of a red blood-cell, containing a large nucleus, a variable amount of pigment, and one or more "centrosomes," occasionally provided with a terminal flagellum; sometimes non-flagellate and very minute forms were found in the red cells. In a liver puncture, round, clear, and encysted forms occurred, enclosed exceptionally in leucocytes. The patient suffered from irregular fever and anæmia combined with a cystic

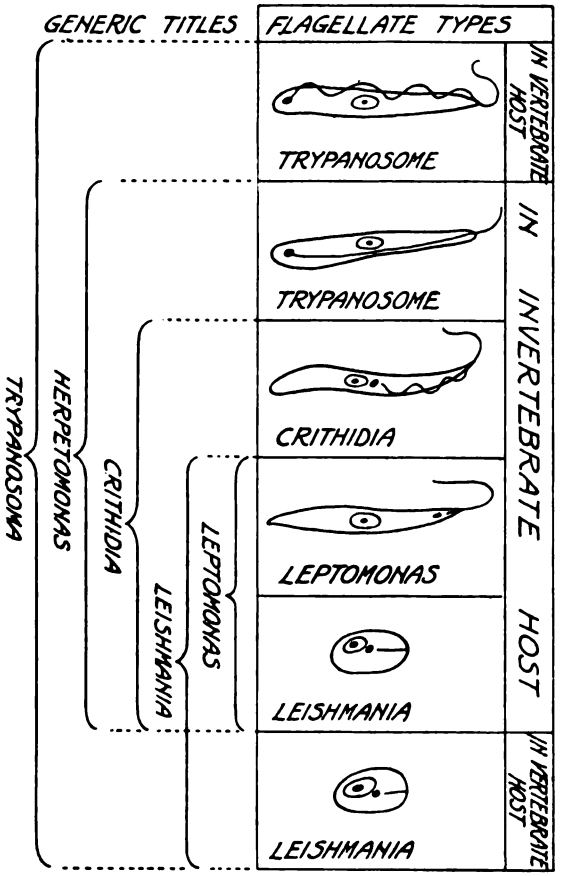


Fig. 250.—Diagram of the classification of the trypanosomes and allied flagellates. (*After Wenyon.*)

enlargement in close proximity to the inferior cervical glands. Liver and spleen were also enlarged.

Histoplasma capsulatum was found by Darling in Panama in the tissues of one Chinaman and two negroes who died of some obscure malady characterized by wasting, irregular fever, enlarged spleen, and anæmia. In smears and sections of the lung, small bodies were found within the epithelioid cells which bore a great resemblance to leishmania, but differed in possessing no kinetonucleus. According to da Rocha Lima the parasite is really a yeast-like organism and has nothing to do with the protozoa, but resembles *Cryptococcus farciminosus*, the cause of epizootic lymphangitis of horses.

Digitized by Google

Order ii.—POLYMASTIGINA

Polymastigina usually possess three or more unequal flagella; a distinct mouth-opening and other organs may also be present. The Polymastigina may be divided into two divisions or suborders—the Tetramitidæ and the Octomitidæ.

SUBORDER 1.—The **Tetramitidæ** usually have three or more flagella arising at the anterior end. A trailing flagellum or an undulating membrane may also be present.

Trichomonas hominis (Davaine, 1860) (Fig. 251).—A common intestinal flagellate of man which inhabits, often in enormous numbers, the large intestine and cæcum. Its body is pear-shaped, 10–15 μ in length by 7–10 μ in breadth. A spherical nucleus is situated in the third anterior end, and just anterior to this are placed three basal granules from which arise three long free flagella; these are directed forwards, while a fourth and thicker one passes backwards and forms the border of an undulating membrane, beyond which it is

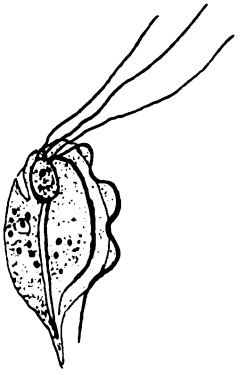


Fig. 251.—**Trichomonas hominis.** × 2,000 diam. (*After Wenyon and Dobell.*)

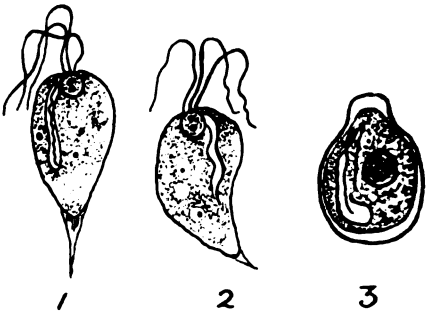


Fig. 252. × 2,000.

1, 2, Active forms of Chilomastix mesnili. (*After Wenyon and Dobell.*)
3, Cyst of the same. (*After Dobell.*)

continued as a free flagellum. A small aperture near the anterior end represents the mouth. A stiffening rod supports the undulating membrane and arises from the blepharoplast. Running down the middle of the body is a second skeletal rod known as the axostyle. The cytoplasm is vacuolated and contains bacteria and food granules.

These flagellates progress rapidly by lashing movements proceeding from the three anterior flagella, while the undulating membrane causes the parasite to revolve on its longitudinal axis. The parasite is also capable of a certain amount of amœboid movement, which is especially seen in degenerating individuals.

Reproduction is effected by longitudinal fission. When completely duplicated, the body of the flagellate splits and gives rise to two daughter individuals. No encysted forms are known, though it seems they must be present at some stage.

Another species of *Trichomonas* occurs in the mouth cavity and on the surface of the tonsil. According to Wenyon and O'Connor, intestinal infections with this parasite are very persistent. They may be present for

Digitized by Google

weeks, disappear from the stools mysteriously, and return just as mysteriously at some later period. There is no evidence that it is pathogenic; its presence in diarrhœic fæces is probably only accidental, as it finds in the liquid stool a congenial medium for multiplication. In dysenteric stools containing blood these flagellates not infrequently ingest red cells.

Varieties of *Trichomonas* occur; those with four or five anterior flagella have been termed *Tetra-* and *Pentatrichomonas*.

Chilomastix mesnili, (*Tetramitus mesnili*), Wenyon, 1910 (Fig. 252), also occurs in the bowel, and resembles *Trichomonas hominis* in general shape and size. It has three long anterior flagella, but is devoid of the large undulating membrane and axostyle. It possesses a large mouth, occupying two-thirds of the body length, with a contained flagellum which, in common with the three anterior organs, arises from a granule situated anteriorly to the spherical nucleus. There is said to be a short undulating membrane in the mouth. The posterior extremity is drawn out to a fine point. The cytoplasm is vacuolated and may contain bacteria, which form the food supply. These organisms vary much in length, but average 14 μ in length by 5–6 μ in breadth. Division probably takes place by longitudinal fission. The lemon-

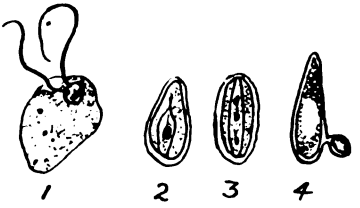


Fig. 253.—× 2,000 diam. (*After Dobell and Wenyon.*)

1, Embadomonas intestinalis; 2, 3, cysts of same; 4, yeast organism simulating an embadomonas cyst.

shaped cysts vary in length from 7–10 μ, contain a single nucleus, and show vestiges of a mouth structure as in the free form. In fresh preparations they have to be differentiated from the yeasts of similar size and shape which are frequently present in fæces.

In freshly voided discharges *Chilomastix* has an active jerky movement, which distinguishes it from the more deliberate rotatory action of *Trichomonas*. Infections with this parasite are very persistent, though there is no evidence that it is pathogenic.

Embadomonas (= Waskia) intestinalis, Wenyon and O'Connor, 1917 (Fig. 253), is a small active flagellate of oval shape, 4–9 μ in length and 3–4 μ in breadth, inhabiting the intestinal canal of man. There are two flagella, the anterior being the longer and thinner; the posterior projects from a mouth situated somewhat laterally at the anterior end. These flagella act independently of each other, thereby imparting a peculiar jerky movement to the organism. In shape it is ovoid, possessing a blunt anterior and a posterior pointed extremity. The cytoplasm is vacuolated and contains ingested bacilli. The round nucleus occupies the anterior end of the body. The cysts are pear-shaped, 4·5–6 μ in length, and when viewed in the fresh state appear to be structureless; when stained, certain nuclear structures can be made out.

This parasite has no pathological significance.

Digitized by Google

Craigia (Paramœba) hominis, Craig, 1906.—This non-pathogenic parasite was first described by Craig in the fæces of soldiers in the Philippines. It occurs as an amœboid organism 10–15 μ in diameter, as a spherical flagellate from 10–20 μ in diameter which is provided with a single flagellum, and also in an encysted stage. It has a single refractile, spherical nucleus which, in the flagellated form, is situated near the flagellum. The amœboid form apparently becomes encysted and ultimately breaks up into a number of flagellated individuals. Reproduction takes place by binary fission.

SUBORDER 2.—The **Octomitidæ** also occur in the intestine. They have eight flagella, arranged in pairs; the body is bilaterally symmetrical in structure.

Giardia intestinalis (= **Lamblia intestinalis**), Lambl, 1859 (Fig. 98, p. 469).—This parasite lives in the upper part of the small intestine. In shape it resembles the half of a pear split longitudinally; it measures 12–18 μ in length by 6 μ in breadth. The ventral surface has a concave sucking disc, with a raised edge, at the anterior end. The posterior extremity tapers into a tail and terminates in two flagella. There are four pairs of flagella, all of which arise from a pair of rod-like organs, the axostyles, running down the centre of the body. Two oval nuclei are situated at the anterior end. This flagellate swims rapidly, swaying from side to side. According to Wenyon and O'Connor, *Giardia* reproduces itself by a very complicated process of binary fission. The cysts may occur in enormous numbers in the fæces. At first binucleate, certain complicated changes proceed inside the cyst wall, which result in the formation of four nuclei, a double axostyle, and finally in two completely new individuals. The cysts are then very characteristic structures, 14 μ in length. The cytoplasm is quite transparent, and the structures contained therein can be defined with precision. The presence of the axostyles, which form a sort of dividing line within the cyst wall, gives it a distinctive appearance, and serves to distinguish it from cysts of the amœbæ.

Giardia is a very persistent infection; cysts may be found in the stools for several years. Under certain conditions it is thought by some observers that this parasite may assume a pathogenic rôle.

CLASS III.—SPOROZOA

This class contains four orders of interest:

i. Gregarinida.
ii. Coccidia.
iii. Hæmosporidia.
iv. Neosporidia.

Order i.—GREGARINIDA

This order contains the Gregarines. Though not of medical, these parasites are of protozoological interest, and are therefore considered in this section. They are found commonly parasitic in the digestive tract of insects, and are not known to occur in the vertebrata. The young organism is at first a parasite of the epithelial cells, but later may become free in the body cavity or in the intestinal canal. The full-grown parasite is of large size, and has a definite shape and cuticle. The anterior end of the body may be provided with a rostrum, termed the *epimerite*, armed with hooks and processes; the posterior portion of the body may be divided by a single septum into two segments, known as the *protomerite* and the *deutomerite*; the nucleus, often

Digitized by Google

of a large size and oval shape, is situated in the latter portion. The complete parasite is capable of independent worm-like motion.

The Gregarines are divided into two groups, in one of which, Eugregarinæ, sexual reproduction only takes place. In the other, Schizogregarinæ, multiplication is effected by both sporogony and schizogony.

The Eugregarines are further divided into two groups, the cephaline and acephaline gregarines. The cephalines have a well-developed epimerite; the acephalines have none, and the body is not segmented.

In the sporogonic phase two full-grown gregarines approximate to one another, become rounded, and secrete a tough common envelope. Each gregarine breaks up into a number of gametes which conjugate in pairs. The resulting zygotes (sporoblasts) each encyst in a sporocyst in which eight sporozoites are formed; these on entering a new host develop into adult gregarines. The whole cycle takes place within the same host.

As an example of the **Eugregarines** the life-history of **Lankesteria culicis** (Ross, 1898) (Fig. 254) is of interest to the tropical student, as it is

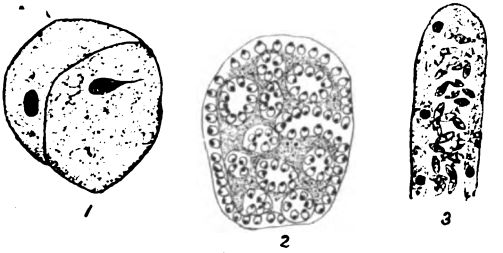


Fig. 254.—Lankesteria culicis (Ross, 1898). (*After Wenyon.*)

1, Two gregarines encysted in Malpighian tube of pupa; 2, gregarine cyst from Malpighian tubes, showing formation of gametes; 3, Malpighian tube of imago of Stegomyia fasciata, showing liberated gregarine sporocysts.

parasitic in the larvæ, pupæ, and imagines of *Stegomyia fasciata*, and may be encountered during the dissection of that insect. It is also of historical interest because it was originally described by Ross during his classical researches into the development of the malaria parasite. Its life-history has been worked out by Wenyon. In the gut of the larva of *Stegomyia* the free gregarines are found, about 50 μ in length, but remain as intracellular parasites during nearly the whole of their trophic development. During the pupal stage the gregarines migrate into the Malpighian tubes, within the cells of which application between two separate organisms takes place and a commensal cyst wall is developed. The body breaks up into a number of gametes, and cross-conjugation takes place, with the formation of sporocysts, each containing eight sporozoites. As a rule, the whole process of development from encystment to the formation of ripe sporocysts takes place during the pupal stage of *Stegomyia fasciata*; in the newly hatched adult mosquito one finds the Malpighian tubes containing gregarine cysts filled with ripe sporocysts. These break loose when ripe, are expelled with the fæces, escape into the water, and are taken up by the newly hatched larvæ.

Order ii.—COCCIDIA

This order also consists of intracellular parasites. There is an alternation of generations, non-sexual schizogony alternating with a sexual cycle in

Digitized by Google

which a number of spores are produced within a cyst, itself the development of a single zygote.

The Eimeria are divided into a number of suborders, amongst which are the Eimeriidea (or true Coccidia) and the Hæmogregarinidæ.

SUBORDER EIMERIIDEA.—The typical life-cycle of a coccidium is exemplified by that of *Eimeria schubergi* in the centipede *Lithobius forficatus*. The young parasites, or sporozoites, are liberated from a spore in the intestinal tract and penetrate epithelial cells, where they grow into large schizonts, characterized by a large vesicular nucleus and a karyosome (nucleolus). When full grown the nucleus divides by repeated fission till a variable number are produced. The schizont now divides into as many merozoites as there are nuclei, and is then full grown. The cells burst, the merozoites are set free, and, entering other cells, develop in one of two ways, either into schizonts again or into gametocytes. The sexes of the latter can be distinguished; in the male the protoplasm is clear, but in the female it is crowded with reserve food material.

The male develops further; the nucleus divides repeatedly, forming many secondary nuclei, which develop into microgametes—small, slender bodies provided with two flagella. The host cell then bursts, liberating the microgametes, which endeavour to enter the female cell or macrogamete. When one such has effected its entrance the macrogamete secretes a tough membrane and becomes an oöcyst, thus effectually preventing the entrance of any other microgametes. The penetrating microgamete fuses with the female nucleus, forming a synkaryon. The zygote breaks up into four sporoblasts; each sporoblast then becomes a spore, surrounded by a tough envelope, the sporocyst, within which the protoplasm divides to form two sporozoites. Therefore, when sporogony is complete, the original oöcyst contains four sporocysts, each containing two sporozoites. In order to develop further the oöcyst must pass out with the fæces and be swallowed by a new host, whereupon the tough membranes dissolve, liberating the sporozoites. (Fig. 255.)

Coccidia are common parasites of vertebrates (rabbits and fowls), and since Wenyon's discovery of the cysts of *Isospora* in human fæces, in 1915, and Dobell's classical work on the same subject (1919), it is known that at least three different coccidia—one *Isospora* and two of the genus *Eimeria*—lead a parasitic existence in man.

Human Coccidiosis

Isospora hominis (Rivolta, 1878), Dobell, 1919 (Fig. 256, 1, 2).—According to Dobell, this species was originally discovered in the villi of the human small intestine by Kjellberg, but its oöcysts and spores were recognized and described for the first time by Wenyon in 1915. Since that date over fifty cases of infection have been recorded. *I. hominis* is by no means a common infection, having been found in but a very small percentage of all diarrhœic cases from Egypt and Gallipoli. There is no proof up to the present that it is pathogenic to man; even in the most heavily infected cases no recognizable symptoms have been described. The Editor has encountered it on seven different occasions in both bacillary and amœbic dysentery stools, as well as in perfectly normal individuals. Feeding experiments in cats and mice have so far failed. The schizogonic cycle of development in the intestine is unknown. The oöcysts are an elongated oval in shape, with a tapering extremity. They vary in length from 25–33 μ, their width being 12·5–16 μ. The cyst wall is perfectly clear and colourless. These cysts are usually discharged in a

Digitized by Google

unsegmented condition, but may contain sporoblasts. In the fæces outside the body they segment into two ovoid spores, each measuring about 14 μ in length by 7–9 μ in breadth, and each containing four sporozoites.

Eimeria wenyoni, Dobell, 1918 (Fig. 256, 3).—This species was discovered by Wenyon in 1916. The oöcysts are passed in the fæces with spores and sporozoites fully developed. The cysts are approximately spherical in shape, with a diameter of 20 μ; the outer surface is rugose, the inner smooth and lined with a delicate membrane. The four oval spores within the cyst

Fig. 255.—Life-history of Coccidium. (*After Schaudinn.*)
1–4, Schizogonic cycle; 5–15, sporogonic cycle.

wall measure 10 μ by 7 μ, and each contains two typical sporozoites. Very few human infections with this organism have, so far, been recorded.

Eimeria oxyspora, Dobell, 1918 (Fig. 256, 4).—This parasite has been found in human fæces by Dobell on one occasion only. The spherical oöcysts measure 36 μ in diameter, and have their contents completely differentiated into four spores, 30 μ in length by 7·5 μ in breadth. Each in turn contains two long slender sporozoites. As in the case of the other species recorded, there is no evidence of pathogenicity.

Digitized by Google

Finally, from the records of Gubler, Leuckart, and Silcock, it is possible that a coccidial parasite occurs very rarely as an hepatic infection in man.

Suborder Hæmogregarinidæ.—These are blood parasites of certain mammals and reptilia, and are included for academical reasons, as they have been several times, though on unsatisfactory evidence, described in man. Their life-cycle in many particulars resembles that of certain coccidia, but differs in that the sexual cycle is passed in an invertebrate host. The Hæmogregarines are found in all classes of vertebrates, and are especially common in reptiles, amphibia, and fishes, but are also found in certain mammals.

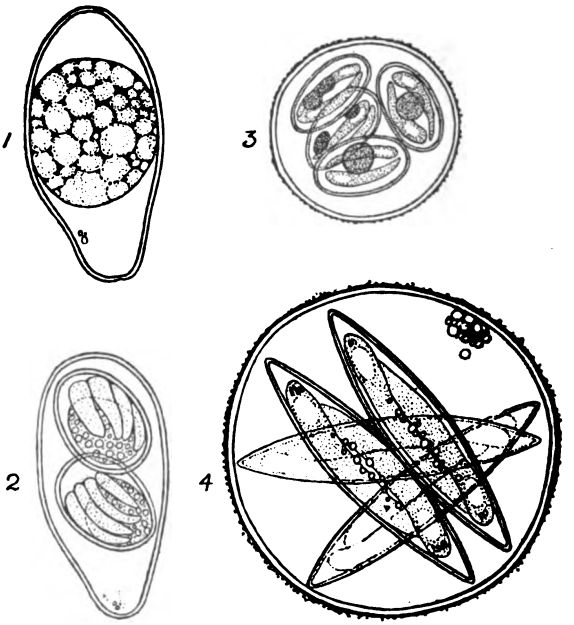


Fig. 256.—Coccidia. × 1,000 diam. (*After Dobell.*)

1, Isospora hominis, undeveloped cyst; 2, fully developed spores of same; 3, Eimeria wenyoni, fully developed oöcysts and spores; 4, Eimeria oxyspora, fully developed oöcyst and spores.

such as dogs, rats, and the jerboa. They are sausage-shaped bodies with a large central nucleus, and lie encapsuled in the red blood-cells or even in the leucocytes (*H. canis*, Fig. 257, and *H. muris*). They are not amœboid, and no melanin is produced. The form seen in the peripheral blood may be liberated from the corpuscle as a free vermicule much resembling a small gregarine in appearance and in its gliding movements. Schizogony does not proceed in the blood, but, as in the case of the subtertian malaria parasite, in some internal organ—in the bone-marrow in some animals; but in the case of *H. jaculi* of the jerboa (Fig. 260) and *H. muris* of the rat, in the liver cells. A variable number of merozoites are produced. Two distinct types of merozoites are formed within different cells. In one type

Digitized by Google

they are numerous and slender, and are then termed *micromerozoites;* in the other they are few in number and stout, and are then called *macromerozoites.* The former, re-entering red cells, are destined to become gametocytes; the macromerozoites may again repeat the cycle and become once more macromerozoites or micromerozoites.

Fig. 257.—Hæmogregarina canis: endocellular in leucocytes and free forms. (*After Wenyon.*)

Fig. 258.—Hæmogregarina seligmanni: encysted, showing operculate capsule. (*After Sambon.*)

Fig. 259.—Hæmogregarina seligmanni: free form. (*After Sambon.*)

The gametocytes appear in the circulating blood, but only develop further in the invertebrate host. In the intestine of the invertebrate they give rise to male and female gametes, and, having escaped from their cells as motile vermicules, become approximated. In the case of *H. stepanowi* of the

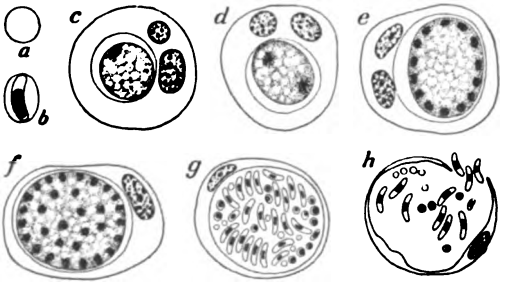


Fig. 260.—Hæmogregarina jaculi. (*After Balfour.*)

a, Normal erythrocyte of jerboa; *b*, infected erythrocyte; *c–h*, schizogony within liver cells.

tortoise the invertebrate host is a leech. Four microgametes are produced by the male gametocyte, and one of these fuses with the macrogamete. The zygote then encysts, and grows into a large oöcyst containing sporozoites, which again pass into the tortoise. The exact manner in which this is effected is not known, but in the case of *H. muris*, which develops in the rat-

Digitized by Google

mite (*Lelaps echidninus*), the mite is devoured by the rat, and the sporozoites, liberated in the rat's intestine, pass through the wall of the gut into the bloodstream, re-enter the liver cells, and become schizonts.

In the leucocytic gregarines, of which the best-known is *H. canis* (Fig. 257), described by James, Christophers, and Wenyon, schizogony takes place in the bone-marrow and spleen of the dog, and is, as described above, of two distinct types. The macromerozoites in this case pass into the blood, are taken up by the leucocytes, and become gametocytes. Sporogony takes place in the body tissues of the tick *Rhipicephalus sanguineus*. The dog probably becomes infected by eating the tick. Practically every dog in Mesopotamia is infected with this parasite, and it is desirable that the student should familiarize himself with its appearance in the routine examination of dogs' blood.

Order iii.—Hæmosporidia

These organisms are parasitic during the whole of their life-cycle; but they exhibit, as do the hæmogregarines, an alternation of hosts, sporogony taking place in the digestive tract of some invertebrate.

The order comprises the genera *Plasmodium*, *Hæmoproteus*, *Leucocytozoon*, and *Piroplasma*.

1. The Genus Plasmodium

In this genus the young schizonts occur within red blood-cells, exhibit amœboid movement, and produce a pigment called "melanin." The invertebrate host is generally a mosquito. Such are the parasites of human malaria—the benign tertian *Plasmodium vivax* (Fig. 261), the quartan *Plasmodium malariæ*, and the pernicious or subtertian *Laverania malariæ* (also known as *Plasmodium falciparum*) (Fig. 262). All these human parasites undergo sporogony in mosquitoes of the genus Anopheles. Similar parasites are found in monkeys (Fig. 263), antelopes, bats, and squirrels. In birds an analogous and pathogenic parasite is known as *Proteosoma* (*Proteosoma grassii*, Labbé, 1894), but, in contradistinction to the human malaria parasite, it is transmitted by mosquitoes of the genus *Culex*, as well as by *Stegomyia fasciata*.

The life-cycle of these parasites (Fig. 261) is now well known and has already been described in detail (p. 19). The sporozoites, minute slender organisms, are introduced into the blood of the vertebrate by the proboscis of the mosquito, and enter red corpuscles. The young parasite, when appropriately stained, is characterized by its signet-ring appearance, there being a large unstained space in the centre of the body. As the parasite grows, this space disappears and the pigment is deposited in the protoplasm. When full grown, multiplication by schizogony takes place. The nucleus, hitherto single, multiplies by repeated division, each daughter nucleus becoming the centre of a merozoite. A blood-corpuscle containing a number of such merozoites represents the characteristic rosette of the malaria parasite. The host cell then ruptures, setting free the merozoites; these penetrate other corpuscles and may grow into either schizonts or gametocytes. The gametocytes are either male or female: the male forms have a large nucleus and a hyaline faintly-staining protoplasm; the female forms have a smaller nucleus and a deeply-staining protoplasm. They are capable of further development only if taken up by the specific kind of mosquito. In the male the nucleus divides, and the daughter nuclei proceed to the periphery of the cell and become nuclei of a number of fine filaments endowed with motile powers, which break free from the cell as microgametes. In the meantime the female gametocyte becomes a macrogamete, and ready for fertilization by the microgamete. The impregnated female gamete, or zygote, is capable of independent movement, and (now termed an oökinete) bores its way through the lining epithelium of the mosquito's stomach, there encysts between the epithelium and the limiting membrane, and becomes an oöcyst.

Digitized by Google

The original nucleus now divides, and the protoplasm segments round the daughter nuclei, forming a spongioplasm. Sporoblast formation, as was formerly described, does not occur (Wenyon). Eventually the nuclei arrange themselves on the surface of the cytoplasm; from this mass sporozoites are

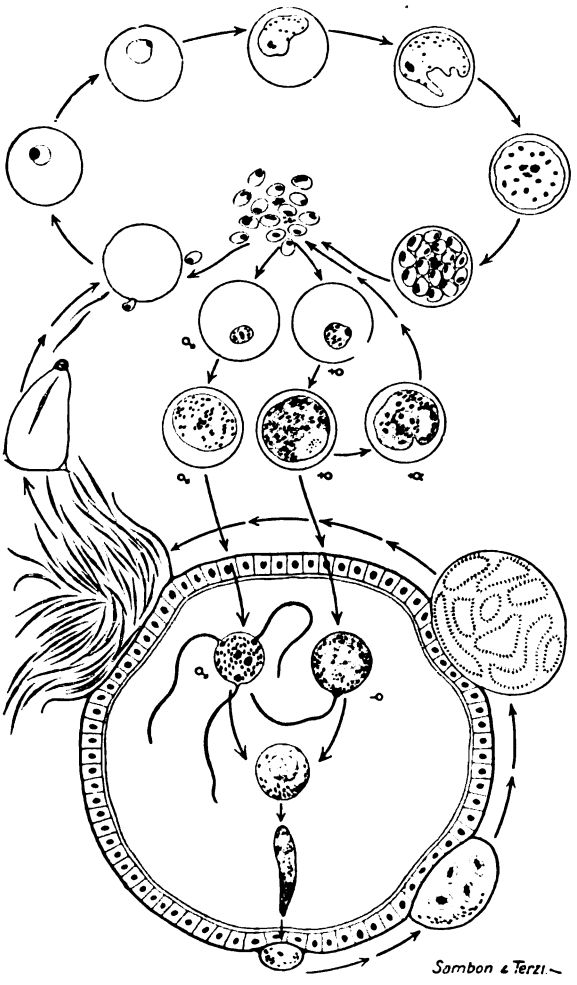


Fig. 261.—Plasmodium vivax: schema of entire life-cycle.

formed, each nucleus acquiring an appropriate quantity of cytoplasm. The oöcyst then bursts, setting free the sporozoites, which contrive to pass into the salivary glands of this insect, whence, with the salivary secretion, they once more enter the blood on which the infected mosquito is feeding.

In the avian red blood-corpuscle the young sporont of Proteosoma

Digitized by Google

displaces the nucleus of the cell to one side in its growth, and thus may be distinguished from a similar stage in Halteridium.

A form of pigment-producing plasmodium occurs in the blood of reptiles and is known as *Hæmocystidium* (Fig. 264). These parasites are of large size, are very numerous in the blood, and do not form microgametes when the blood is drawn.

Toxoplasma is a parasite of small size inhabiting the endothelial cells of the peritoneum, and mono- and polymorphonuclear leucocytes. It has been found in pigeons, the dog, the mole, the rabbit, and in a rodent called the gondi (*Ctenodactylus gondii*) by Nicolle in Tunisia. Multiplication takes place by binary fission; the nucleus is single; no kinetonucleus is present. From its morphological characteristics it is apparently allied to the Hæmosporidia.

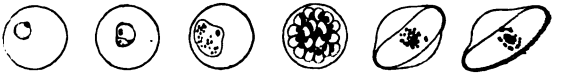


Fig. 262.—Laverania malariæ.

2. The Genus Hæmoproteus

Members of this genus (also termed *Halteridium*) are parasitic in the blood of many widely different species of birds. Within the red blood-corpuscle they grow into a characteristic dumb-bell-like shape, partially enveloping but not displacing the nucleus of the corpuscle. In the halteridium of the pigeon (*Hæmoproteus columbæ*) the sexual cycle is passed in a hippoboscid fly, *Lynchia maura*, and is similar to the one already described. Schizogony takes place within a capillary endothelial cell of the pigeon, but the parasites are afterwards found within leucocytes in the lung capillaries. In the leucocytes the parasites grow and divide into a number of small forms

Fig. 263.—Plasmodium kochi, from a monkey (Cercopithecus sabæus). (*After Lühe.*)

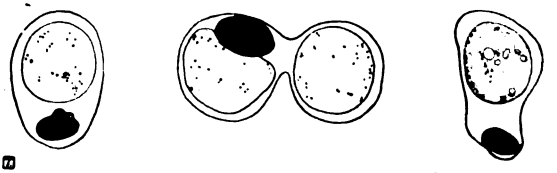


Fig. 264.—Hæmocystidium simondi.

or merozoites; finally the leucocyte bursts, setting free the merozoites, which, entering red blood-corpuscles, assume once more the typical shape of the sporonts. The male gametocyte is easily distinguished from the female by the larger size of its nucleus and by the faintly-staining properties of its protoplasm.

The life-cycle as worked out by Schaudinn was of an entirely different character. It is now known that the blood of *Athene noctua*, the little owl, with which Schaudinn worked, contains

Digitized by Google

a number of blood parasites, namely, a proteosoma, a halteridium, two trypanosomes, a leucocytozoon, and a spirochæte. Schaudinn held that the trypanosomes, the leucocytozoon, and the spirochæte formed different stages of the same life cycle.

3. The Genus Leucocytozoon

The genus *Leucocytozoon* of Danilewsky must be carefully distinguished from the leucocytic hæmogregarines to which allusion has already been made. The leucocytozoa are elongated oval bodies (Fig. 265), parasitic in the blood of birds. They modify the shape of the host cell, generally a mononuclear leucocyte. Male and female forms are recognized; in the latter the protoplasm acquires a deep stain; no pigment is formed. Schizogony takes place

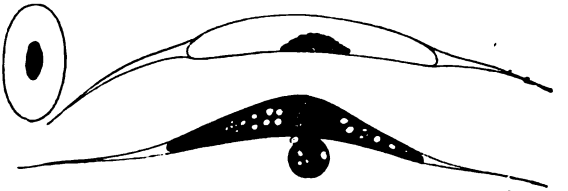


Fig. 265.—Leucocytozoon neavei, from the guinea-fowl. (*After Neave.*)

in the spleen of the bird. "Exflagellation" and fertilization occur exactly as in the malaria parasite, but the method of transmission and the definitive host are still unknown.

4. The Genus Piroplasma

This genus consists of a number of minute oval organisms, several of which are often contained in the one red blood-corpuscle. No pigment is produced, but the corpuscle is destroyed, the hæmoglobin set free and ultimately partly excreted by the kidneys of the host.

The best-known piroplasm is *Piroplasma bigeminum* (or *Babesia bovis*), the parasite of red-water or Texas fever of cattle.

Fig. 266.—Piroplasma canis. (*After Nuttall.*)

Piroplasma caballi causes biliary fever in horses; *Piroplasma canis* (Fig. 266), malignant jaundice in dogs; while *Piroplasma mutans* is apparently a harmless parasite in the blood of African cattle.

The typical piroplasma is a pear-shaped body dividing by a process of budding, and is found in the red corpuscles of oxen, of sheep, and of a number of wild animals.

The genus Piroplasma has, for convenience' sake, been divided into a number of subgenera of doubtful validity.

Theileria is the title reserved for a number of bacillary or coccoid forms. *Theileria parva* (Fig. 267) is the parasite of "East Coast fever" of African cattle. *P. mutans* is commonly found also in the blood of cattle suffering from "East Coast fever," but is apparently non-pathogenic. In *Th. parva*

Digitized by Google

the forms in the blood consist entirely of gametocytes; in *P. mutans*, on the other hand, the quadruple forms in the erythrocytes apparently represent a stage of the schizogony. Therefore direct inoculation of blood containing *Th. parva* does not produce the disease, whereas infection with *P. mutans* invariably succeeds, if schizonts of this species are present in the inoculating blood. The schizogonic stage of *Th. parva* is apparently passed in the internal organs such as the spleen. Splenic puncture in the diseased animals reveals bodies bearing a rough resemblance to a multiplying quartan malaria parasite known as "Koch's bodies"; it is thought that these bodies, which are capable of reproducing the disease on re-inoculation, represent the schizogonic cycle in the splenic cells.

Nuttallia is a small oval or pear-shaped piroplasm, which in multiplying sometimes assumes the form of a cross. Two kinds are known: one, *N. equi*, causes piroplasmosis in horses in southern Europe; the other, *N. herpestidis*, is found in the mongoose.

Anaplasma, a small coccoid body in the red cells, has been described by Theiler in cattle. These bodies are arranged either in the centre of the cell or radially; hence the names *A. centrale* and *A. marginale* have been applied to them. According to recent investigations they are not parasites at all, but merely represent a degeneration of the red cell.

Within the red cell the piroplasm consists of little save vacuolated protoplasm and a simple nucleus. The parasites are said to exhibit a certain amount of amœboid movement, and, when free from the cell, to be capable

Fig. 267.—Theileria parva. (*After Theiler.*)

of independent locomotion. The development in the vertebrate host appears to proceed solely by either binary or quadruple fission.

The transmission of the piroplasms is effected by ticks; in the case of *P. bovis* it is adapted to the life-history of the transmitting tick (*Ixodes reduvius* or *Margaropus australis*), and in *P. canis* to *Rhipicephalus sanguineus*. The tick is hatched first as a minute six-legged larva, which becomes an eight-legged nymph, differing from the adult only in the absence of genital organs. In each stage the tick feeds on vertebrate blood but once. The infection is passed to its ova by the infected female tick. The developmental stages of this parasite in the tick are little known. Apparently, according to Christophers and Koch, the parasites escape from their red cells and become transformed into star-shaped bodies representing the gametocytes. Conjugation of these bodies takes place, and when complete the zygote becomes a motile body resembling an oökinete. The oökinetes apparently penetrate into the ova of the tick, wherein they assume a globular shape. When the egg hatches into a six-legged larva, these bodies break up into a number of sporoblasts, which become scattered throughout its tissues. The sporoblasts divide in turn into a number of sporozoites resembling the pear-shaped forms seen in the blood; these, according to Christophers and Gonder, contrive to enter the salivary glands, and thus re-enter the bloodstream when the tick becomes adult and again feeds on blood. (Fig. 268.)

Certain rod-shaped bacilliform bodies have been described in red cells of rats, moles, and gerbyls, and the Editor has found similar piroplasma-like

Digitized by Google

bodies in the *Spalax* in Syria; their protozoal nature is doubtful, but they are possibly of the same nature as the structures met with in Oroya fever and known as *Bartonella bacilliformis*. (Fig. 269.)

Order iv.—NEOSPORIDIA

Parasites belonging to this order complete their development within the body of one host. The adult parasite is incapable of independent movement. There is often a plasmodial intracellular stage in which spore-formation is commenced and is continued throughout the life of the parasite. The order is divided into three suborders: (1) the Cnidosporidia, characterized by the

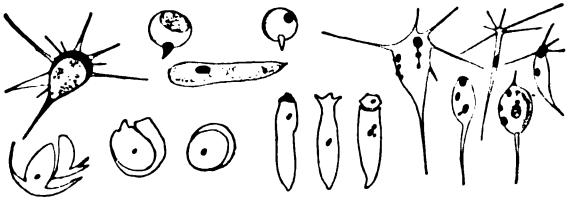


Fig. 268.—Developmental forms of Piroplasma canis in tick's gut.
(After Koch, Klein, and Christophers.)

possession of polar capsules in the spores; (2) the Haplosporidia, in which those features are absent; (3) the Sarcosporidia.

The life-history of *sarcocystis tenella*, a sarcosporidian, will be considered. It is a parasite of sheep and cattle, occurring as a cystic white body, known as "Miescher's tubes," visible to the naked eye in the striped muscles. As a rule it produces no symptoms. The cyst contains a number of crescentic bodies (spores): each spore is provided with a nucleus situated at the blunt end. In this species the mode of propagation from one host to another is

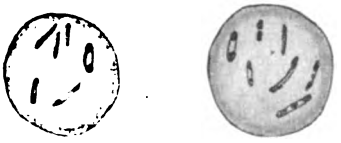


Fig. 269.—Grahamella, or bacilliform bodies in red cells of rat, mole, etc. *(Orig.)*

unknown, but mice can be infected by feeding on the bodies of others harbouring *S. muris*; apparently in this case the spore germinates in the intestine of its host and sets free an amœbula which eventually reaches the striped muscle, where it grows into the adult sarcocyst. According to Blanchard, Darling, and others, several species of sarcocystis have been found as accidental infections in man as a result of ingestion. *S. tenella* and *S. muris* have been found in the vocal cords.

Of the Haplosporidia, one, *Rhinosporidium seeberi* (= *kinealyi*), is found in man in India. It gives rise to polypoid outgrowths from the septum nasi. The youngest parasites appear to be round cells provided with a cuticle and a single nucleus. By repeated division of this nucleus the parasite becomes

Digitized by Google

a multinucleate plasmodium. The cyst contents become divided into spores. When ripe the cyst bursts and scatters its contents into the surrounding tissues.

Nothing is known of the transmission of this parasite or the manner in which infection is acquired.

Class IV.—CILIOPHORA

The Ciliate Protozoa parasitic in man are represented by **Balantidium coli**, an oval-shaped parasite belonging to the subclass Ciliata. The parasite measures about 30–200 μ in length by 20–70 μ in breadth. The body is clothed with a thick covering of cilia. There is a large kidney-shaped meganucleus with a small micronucleus approximated to it. The protoplasm contains two contractile and a number of food vacuoles, and there is a definite anteriorly-situated mouth. Nutrition is effected by ingestion of solid particles. The cuticle is longitudinally striated. The parasite reproduces itself asexually by transverse fission. Conjugation takes place by approximation of two individuals and by the exchange of certain nuclear elements; after this has been effected the conjugants separate. Encystment may take place. (Fig. 97, p. 467.)

Balantidium coli sometimes burrows into the submucosa and causes dysenteric symptoms known as balantidium dysentery (*see* p. 466). It is a normal inhabitant of the large intestine of pigs, and those who are in attendance upon them are liable to infection. It has been found in the mesenteric glands as well as in the ulcers. It is a very active and obvious parasite, and may occasionally be found in diarrhœic as well as in blood and mucous stools.

Infection with this organism has been recorded from France, Germany, the Philippines, and elsewhere. The parasite also occurs in monkeys.

THE CHLAMYDOZOA

A name proposed by Prowazek to include a number of doubtful organisms. These problematic bodies are so minute that they are said to pass through a bacterial filter. They are parasites of cells, but according to some authorities they merely represent a nuclear degeneration.

It is enough to mention that such diseases as vaccinia, variola, trachoma, epithelioma contagiosa of birds, verruga Peruviana, molluscum contagiosum, measles, and foot-and-mouth disease of animals, have been ascribed to the agency of these Chlamydozoa.

THE SPIROCHÆTES (*see* Fig. 65, p. 212).

Seeing that systematic biologists were unable formerly to agree as to the group of the Protista in which spirochætes should be placed, the classification of these flexible spiral organisms has been a matter of considerable difficulty till comparatively recently.

Although it has now been conceded that on general as well as on morphological grounds they should be classified among the bacteria, it is advisable to give some account of the more recent views of classification according to Dobell.

The genus **Spirochæta** (Ehrenberg, 1834) includes certain large free-living fresh-water or marine species, of which *Spirochæta plicatilis* is the type. This organism measures up to 500 μ in length and 0·75 μ in breadth. It is a cylindrical filament with regular spirals about 1·5 μ apart. It has an elastic

Digitized by Google

flexible axial filament, and possesses no crista or flagella. It is not dissolved by 10-per-cent. bile salts or saponin, according to Noguchi.

The genus **Saprospira** (Gross, 1911) contains large free-living marine and fresh-water spirochætes, of which *Saprospira grandis* is the type. This measures up to about 100 μ in length and 0·8 μ in breadth, and is divided internally into chambers by many transverse septa. The organism is disposed in numerous relatively rigid undulating curves. There are no flagella, nor is there a crista.

The genus **Cristispira** (Gross, 1910) is reserved for certain large spirochætes maintaining a parasitic existence in the alimentary tract of oysters and other shell-fish. The type is *Cristispira balbianii*, an organism 45–90 μ in length and nearly 2 μ in breadth, with rounded ends. It is cylindrical in shape and composed of two to five large irregular flexures. It possesses a distinct and flexible longitudinal crest or crista, and shows an internal chambered structure like the preceding.

The genus **Spironema** (Vuillemin, 1905), of which the type is *Spironema pallidum*, contains species exhibiting a considerable variation in size. The extremities of the organism are pointed and attenuated, the spirals are wavy and regular. No axial filament is present, and no crista or undulating membrane. These organisms are all disintegrated by 10-per-cent. saponin and bile-salts. The smaller and finer species, the organisms of syphilis (*S. pallidum*) and of yaws (*S. pertenue*), are composed of numerous regular corkscrew-like spirals of an amplitude of 1 μ. In length these organisms measure 5–14 μ. Similar non-pathogenic species are found in the human mouth and elsewhere. The larger forms of *Spironema* are more flexible and snake-like and comprise the organisms of relapsing fever (*S. recurrentis*, *S. novyi*, *S. duttoni*, *S. berberum*) in man; *S. gallinarum* and *S. anserinum*, the organisms of spirochætosis of fowls and geese respectively; *S. eugyratum*, saprophytic in human fæces; *S. buccale*, of the human mouth; and *S. refringens*, saprophytic on ulcerating surfaces.

The genus **Leptospira** (Noguchi, 1917) includes the type organism, *Leptospira icterohæmorrhagiæ*. These organisms measure 7–14 μ in length, with pointed ends and a spiral amptitude of 0·45 μ, with one or more gently undulating curves. There is no terminal filament, axial filament, or undulating membrane. They are resistant to 10-per-cent. saponin, but are dissolved by bile-salts. Four pathogenic species are known—*L. icterohæmorrhagiæ* of Weil's disease, *L. morsus-muris* of rat-bite fever, *L. hebdomadalis* of seven-day fever, and *L. icteroides* of yellow fever.

All these organisms divide by transverse division, like other bacteria. Multiple division occurs in *Spirochæta* and *Saprospira*, but simple division into two is the rule in the other forms. A peculiar method of spore-formation has been described in *Cristispira* and *Saprospira*, but is not known to occur in other genera. No sexual phenomena are known in any spirochæte, and the life-histories of all forms appear to be very simple. The Spirochætes, as a group, differ from the more familiar *Spirilla* chiefly in being flexible—not rigid—spirals, and in possessing no true flagella.

Digitized by Google

APPENDIX II

MEDICAL HELMINTHOLOGY, ENTOMOLOGY, ETC.

THIS Appendix contains a brief introduction to the study of systematic zoology viewed from a medical standpoint. Parasites, as for instance the helminths, which are of considerable pathological importance to man, will be treated in some detail, but of the insects only a brief outline can be given.*

Systematic helminthology consists in a study of the phyla Platyhelminthes and Nemathelminthes, the first of which is divisible into three large classes—(1) the Turbellaria, (2) the Trematoda, and (3) the Cestoda. Of the phylum Platyhelminthes only the Trematoda and Cestoda need be considered, as containing genera parasitic in man. The Nemathelminthes are considered at length later.

Methods of preservation.—All worms must be collected into normal saline, and not into plain water. After removal of fæcal matter and other débris they may be preserved by either of the following methods:

1. Transfer to 5-per-cent. formalin solution, or to weak Langeron's lactophenol † if procurable.
2. Kill by dropping into boiling 70-per-cent. alcohol containing 5 per cent. glycerin, and store indefinitely in this medium.

For sending home material for identification and study from abroad it is unwise to use the second method, owing to risks of evaporation and Customs difficulties. Care should be taken to affix the postage-stamps to a label attached to the packet and not on to the packet itself, as the contained bottles may be broken in passing through the post. The specimens should be wrapped in cotton-wool in lactophenol solution inside a wide-mouthed bottle, which in turn should be placed in a wooden box.

PHYLUM PLATYHELMINTHES

Zoologically speaking, the platyhelminths are bilaterally segmented, acœlomate animals in which the alimentary canal may be entirely absent; when present, it has only one aperture to serve both as mouth and as anus.

CLASS II.—THE TREMATODA

These are worms with leaf-shaped and usually flattened bodies. In size they may vary from 0·1 mm. to almost a metre in length. One or more suckers may be present, anterior or ventral in position; the latter are prehensile, the former alimentary in function.

The *alimentary canal* consists of a mouth situated in the oral sucker, a

* For more exhaustive treatises upon the same subjects the reader is referred to the invaluable "Précis de Parasitologie" by Brumpt, 2nd edit., 1913, and Alcock's "Entomology for Medical Officers," 2nd edit., 1920.

† Langeron's lactophenol consists of carbolic acid 1 part, lactic acid 1 part, glycerin 2 parts, water 1 part.

Digitized by Google

muscular pharynx, which may be absent, a thin-walled œsophagus which divides posteriorly into two blind intestinal cæca. Food consists of blood or cells.

The *nervous system* consists of two large supra-œsophageal ganglia joined by a transverse commissure. From these, nerves pass out to other organs.

Excretory system.—The main ducts enter the excretory sac in the median line; this sac discharges by the excretory pore.

The *genital organs* are for the most part hermaphrodite; both sets, male and female, open by a common genital pore. The testes are round, lobed, or branched; the ovary also may be of various shapes. The yolk-glands are much branched, and a shell-gland is also present. The uterus contains many ova, derived from the ovary, and these, when passing down the oviduct, are fertilized by spermatozoa from the receptaculum seminis. Into this organ they find their way in the process of cross-fertilization; autofecundation can occur. Frequently the receptaculum communicates with the exterior by Laurer's canal, opening externally in the middle line. This canal in some cases is also functionally a vagina and serves for the entrance of spermatozoa received in copulation. The fertilized egg receives a supply of yolk from the vitelline duct and glands, and a chitinous shell from the shell-gland. When complete the ovum enters the uterus and passes to the exterior.

All the organs are embedded in parenchyma tissue.

Life-history.—There are two life-cycles: (*a*) *Monogenea*—development into a non-ciliated larva which changes directly into a sexual hermaphroditic animal; (*b*) *Digenea*—development into a ciliated larva which enters into other animals—molluscs, leeches, or fishes, encysts, and takes on a second larval form. The egg consists of a spherical cell surrounded by yolk granules; the cell itself alone undergoes development. The shell is oval, and often is provided with a lid or operculum. When laid, the egg generally contains a ciliated embryo, or *miracidium*, possessing embryonic elements. This miracidium lives in water, in which it swims actively about, and can develop further on entering an intermediary host—generally a fresh-water snail—in the liver or digestive organ of which it becomes a sac-like organism or *sporocyst* containing numbers of germinal cells. Agglomerations of these cells or germinal balls may give rise (*a*) to special larvæ or *cercariæ*, (*b*) to other sporocysts called *daughter sporocysts*, (*c*) to structures—called *rediæ*—provided with an oral sucker and a rudimentary intestine. In the body cavity of these rediæ further cercariæ are produced; moreover the germinal cells inside the original redia may give rise to *daughter rediæ*. (Fig. 270.)

The life-cycle of the Trematoda was formerly looked upon as an alternation of generations of the variety called *heterogony*, but more recent authors regard it as a sexual generation alternating with a parthenogenetic generation, the germinal cells of the sporocyst being regarded as ova developing parthenogenetically. A remarkable adaptation is seen in *Distoma macrostomum* Rud., a parasite of insectivorous birds. The eggs are consumed by a snail, *Succinea amphibia*, in the gut of which the miracidium is set free and, making its way through the gut wall into the tissues, becomes a branched sporocyst. Some of these branches enter the tentacles, to which they give a peculiar appearance by their colouring of green and white bands and red tip. The bird, attracted by the colouring, which resembles a gaily-coloured caterpillar, pecks off the tentacles and so swallows the sporocyst, which contains tailless cercariæ.

The cercariæ are larval trematodes provided with one or more suckers and a tail which serves for progression. Many resemble a minute tadpole.

Digitized by Google

They are set free from the liver or digestive gland of the snail and make their way into the surrounding water, in which they can live for about forty-eight hours. In some instances they shed their tails and pierce the skin of their definitive host, while in others they encyst in another organism, either animal, plant, or fish, and are ingested by their host either during eating or drinking. Once inside the definitive host the immature flukes migrate to their site of election—the liver, the lung, the intestinal canal, or in some instances the bloodstream.

TREMATODES PARASITIC IN MAN

The flukes parasitic in man belong to the groups DISTOMATA and AMPHISTOMATA of the digenetic trematodes.

GROUP	CHARACTERS	GENUS	EXAMPLE
DISTOMATA ...	Intestine branched	*Fasciola* ...	*F. hepatica*
	Intestine simple; genital pore in front of ventral sucker; testicles posterior to uterus		
	(*a*) Large-sized ovary and testicles branched	*Fasciolopsis* ...	*F. buski*
	(*b*) Testicles branched ...	*Clonorchis* ...	*C. sinensis*
	(*c*) Testicles lobed... ...	*Opistorchis* ...	*O. noverca* *O. felineus*
	(*d*) Testicles anterior to uterus	*Dicrocœlium* ...	*D. dendriticus*
	Intestine simple; genital pore posterior to ventral sucker		
	(*a*) Testicles ovoid; body flattened	*Heterophyes* ...	*H. heterophyes*
	(*b*) Testicles ovoid; genital sinus provided with a muscular ring	*Metagonimus* ...	*M. yokagawai*
	(*c*) Testicles lobed; body thick and massive	*Paragonimus* ...	*P. westermanni*
	(*d*) Collar of spines surrounding oral sucker dorsally and laterally	*Echinostomum*...	*E. ilocanum* *E. malayanum*
	(*e*) Sexes separate, intestinal canal terminating in a simple cæcum	*Schistosoma* ...	*S. hæmatobium* *S. mansoni* *S. japonicum*
AMPHISTOMATA	Suckers situated at anterior and posterior extremities of the body; testes anterior to ovary		
	(*a*) Pharynx with lateral pouches	*Watsonius* ...	*W. watsoni*
	(*b*) Anterior sucker situated upon anterior cylindrical cone	*Gastrodiscoides*	*G. hominis*

FASCIOLA HEPATICA (Linn., 1758)

Synonyms.—*Distoma hepaticum; Fasciola humani; Distomum cariæ; Cladocœlium hepaticum.*

History.—There are 28 recorded cases of the erratic occurrence of this parasite in man. It has been found in the liver, the portal veins, and in subcutaneous abscesses; according to Khouri it frequently occurs as a

Digitized by Google

bucoopharyngeal infestation in the Lebanon, where the disease is known as "halzoun."

Geographical distribution.—*F. hepatica* has a worldwide distribution wherever sheep are found.

The parasite.—*F. hepatica* (Fig. 271) is a parasite of herbivorous animals, especially the sheep, in which it causes the disease known as sheep rot. It is a flat and slender fluke with a well-marked cephalic cone; in colour pale grey with dark borders; in length, 20–30 mm.; in breadth, 8–13 mm. The integument is provided with spines arranged in rows. The anterior extremity, which bears the anterior sucker, is narrow; the posterior blunt. The ventral sucker is the larger of the two, and is situated 3 mm. from the former; its opening is triangular in shape. The œsophagus is shorter than

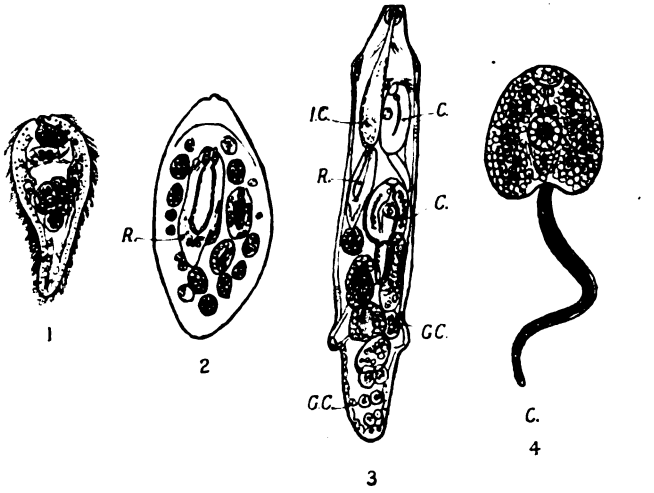


Fig. 270.—Stages in life-history of Fasciola hepatica. (*After Thomas and Leuckart.*)

1, Miracidium; 2, sporocyst with rediæ (*R.*); 3, redia containing daughter rediæ (*R.*), cercariæ (*C.*), and germinal balls (*G.C.*); 4, free cercariæ containing cystogenous cells.

the pharynx; the intestinal canal is furnished with many diverticula radiating outwards. The ovaries ramify and are situated anteriorly to the vitelline ducts. The shell-gland lies near the ovary in the median line, and posterior to this are two much-branched testes.

The life-history of this fluke was first worked out by Thomas and Leuckart in 1883, and has already been detailed (p. 785). The ciliated miracidium escapes from the egg and develops into rediæ and cercariæ in fresh-water snails of the genus Limnæa; in Europe it is *Limnæa truncatula* (or *L. minuta*). Where this species is absent the parasite adapts itself to an analogous species—for instance, *L. oahensis* in the Sandwich Islands; *L. viator* in South America; *L. humilis* in North America.

A large variety of this parasite is found in sheep and goats in Africa, and is known as *F. gigantea*. Examples up to 75 mm. in length have been recorded in man by Gouvea in Rio de Janeiro; the fluke was coughed up from the lung.

Digitized by Google

Pathogenesis.—The disease known as "halzoun" or buccopharyngeal distomatosis, is said to be not uncommon through eating raw livers of goats heavily infested with this parasite. It would appear that the flukes which escape injury during mastication attach themselves to the pharyngeal wall much in the manner of a leech. The symptoms thus produced are extremely varied and may last for several days; they may consist of dysphagia, dysphonia, congestion of the head, and may end in death. After the trematode has become detached through vomiting, convalescence sets in.

Treatment consists in administering emetics and alcoholic gargles, which aid in detaching the parasite.

Fasciolopsis buski (Lankester, 1857)

Synonyms.—*Distoma buski; D. rathouisi; Dicrocœlium buski.*

History.—*Fasciolopsis buski* was first described by Busk in his "Diseases of the Liver," published in London in 1845. Busk found this parasite in

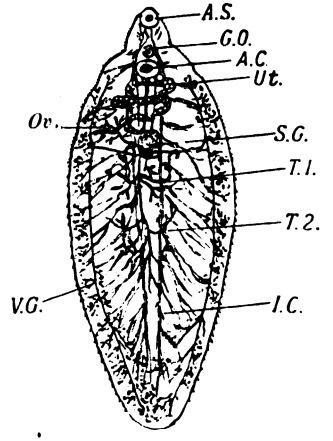


Fig. 271.*—Fasciola hepatica.

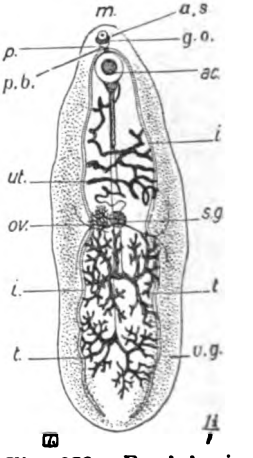


Fig. 272.—Fasciolopsis buski. (*After Odhner.*)

1843 in the duodenum of a lascar who died at the Seamen's Hospital. The pig is the normal host.

Geographical distribution.—*F. buski* is an Asiatic trematode; it has been found in India, Assam, the Straits Settlements, Sumatra, and China.

The parasite (Fig. 272) is the largest trematode inhabiting man. It measures 24–55 mm.; the average is 30 mm. in length (75 mm. according to Busk) by 12–14 mm. in breadth and 2 mm. in thickness. In shape it is an elongated oval, rather narrower anteriorly than posteriorly, with flat ventral surface, slightly convex dorsal surface, and very thin margins.

* The following is a key to the terminology of anatomy of trematodes:—*a.s.*, anterior sucker; *m.*, mouth; *p.*, pharynx; *p.b.*, pharyngeal bulb; *ac.*, acetabulum or ventral sucker; *g.o.*, genital opening; *ut.*, uterus; *v.g.*, vitelline glands; *ov.*, ovary; *s.g.*, shell gland; *va.*, vagina; *oo.*, oötype; *ovd.*, oviduct; *v.s.*, vesicula seminalis; *r.s.*, receptaculum seminis; *t.*, testis; *v.d.*, vas deferens; *œs.*, œsophagus; *i.*, intestine; *i.c.*, branch intestine; *ex.p.*, excretory pore; *n.c.*, nerve cord.

Digitized by Google

has a smooth skin on the dorsal surface. The ventral surface is covered with spines, most numerous in the acetabular region; they are arranged in regular transverse rows. It is deep pink in colour. The oral sucker (0·5 mm. in diameter) is subterminal and placed on the ventral surface. The ventral sucker is larger (1·6–2·5 mm. in diameter) and placed close to the oral. It is prolonged into a kind of sac (2–8 mm. long) directly under the ventral surface. The pharynx (0·7 mm. long) is preceded by a prepharynx (0·28 mm. long); the œsophagus is very short and the intestinal cæca are simple and present two characteristic curves towards the middle line, one at about the middle of the body, the other between the testes. The genital pore opens on the median line immediately anterior to the ventral sucker. The testes are in the posterior half of the body, one behind the other; both are branched dichotomously. The ovary is branched, and is placed about the middle of

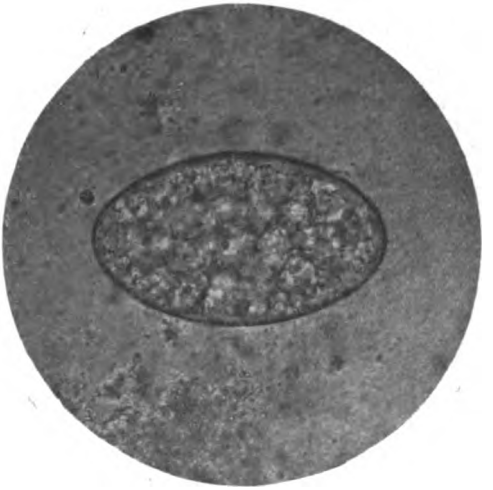


Fig. 273.—Ovum of Fasciolopsis buski. × 250.
(Photograph by Dr. J. Bell.)

the body on the right of the median line. The vitellaria are well developed, and extend from the ventral sucker to the caudal end of the body, where they meet. The acini are very small. The eggs (Fig. 181, *h*, p. 655, and Fig. 273) are numerous and measure 120 to 130 μ in length by 77 to 80 μ in breadth; they are closed by a very delicate operculum.

Varieties of F. buski.—Latterly attempts have been made to split up *F. buski* into various subspecies. For instance, under the name of *F. rathouisi* a fluke was described by Poirier in 1887. The validity of this species has given rise to a great deal of discussion. Odhner, who has examined the type specimen, believes that the so-called distinctive features are solely due to error in the interpretation of serial sections of *F. buski*. The form known as Kwan's fluke was shown by Leiper to be a much-distorted specimen. *F. fülleborni* is said to be larger and more oval in shape.

The life-history of this parasite has not yet been worked out.

Pathogenesis and treatment.—*F. buski* inhabits the upper part of the

Digitized by Google

small intestine. In two recorded instances (Cobbold) it was associated with attacks of recurring diarrhœa and other signs of intestinal irritation. The best treatment is thymol or eucalyptus oil, given as in ankylostomiasis.

Clonorchis sinensis (Cobbold, 1875)

Synonyms. — *Distoma sinense ; D. spathulatum ; D. japonicum ; D. innocuum ; Opisthorchis sinensis ; Clonorchis endemicus.*

History.—*C. sinensis* was discovered almost simultaneously by MacConnell in India and MacGregor in Mauritius, in 1874.

Geographical distribution.—This is a common parasite of man in Eastern countries (*see* p. 651).

The parasite.—*C. sinensis* (Fig. 274) measures 10–20 mm. in length by 2–5 mm. in breadth; it is oblong, narrow, flat and somewhat pointed anteriorly, reddish in colour, and nearly transparent. The oral sucker is larger than the ventral acetabulum, which is situated between the first and second fourths of the body. The cuticle has no spines. The pharynx is globular and short (Fig. 274, *p.b.*), the œsophagus slender and 0·17 mm. long. The bifurcation of the intestine is nearer to the oral than to the ventral sucker. The intestinal cæca are simple, slender, and extend almost to the posterior end of the body. The genital pore opens on the middle line immediately in front of the acetabulum. The testes are branched and situated in the posterior portion of the body, one behind the other. The ovary is trilobate and anterior to the testes. The uterus is moderately developed and its coils are anterior to the genital glands. The vitelline glands are moderately developed and occupy about the middle third of the body. The eggs are 28 to 30 μ in length by 15 to 17 μ in breadth, operculated, almost black, and contain a ciliated miracidium (Fig. 181, *e*). Most probably its immature stages are passed in a mollusc, *Bythinia striatula* var. *japonica* (Pilsbury), and in *Melania libertina* (Muto). Cercariæ of this species are found in Japan in fresh-water fish of the family Cyprinidæ (*Pseudorasbora parva*, *Leucopodia güntheri*), in which they become encysted in the muscles, as in the case of *Opisthorchis felineus*. Recently Yokagawa has found them in two other species of fish, *Leucogobis mayedæ* and *Carassius auratus*, the latter of which is the more important. These fish act only as the second intermediary host; the first is the snail *Bythinia*. Muto has conducted experiments in feeding the definitive host on infested bythiniæ, with a negative result. The encysted larvæ are killed at 100° C., but retain their vitality for at least fifteen minutes at lower temperatures; in vinegar and soy-sauce they survive for five hours. The young distomes are provided with spines which soon disappear, and they attain maturity in twenty-six days, when ova are found in the fæces of cats, dogs, rabbits, and guinea-pigs fed on infected fish.

Kobayashi has found cats infested with this parasite. A smaller variety of *C. sinensis* has been described as *C. endemicus*, but is now recognized as being identical.

Pathogenicity.—This subject is dealt with on p. 651.

Opisthorchis noverca (Braun, 1903)

Synonyms.—*Distoma conjunctum ; Paropisthorchis caninus* (Barker, 1912).

History.—*Opisthorchis noverca* was discovered by MacConnell in Calcutta in 1876, and was first thought to be identical with *Metorchis conjunctus* of the fox, but in 1903 was described by Braun as a different species. It is a parasite of the dog, so far recorded in man only from India.

Digitized by Google

The parasite.—*O. noverca* is of a lanceolate shape, and more attenuated anteriorly than posteriorly. It measures 9–12 mm. in length by 2·5 mm. in breadth. The oral sucker (Fig. 275, *m.*) is terminal and larger than the acetabulum or ventral sucker (Fig. 275, *ac.*), which is situated close to it, just below the bifurcation of the intestine. The cuticle is densely covered with spines. The pharynx (Fig. 275, *p.b.*) is large and globular; the intestinal cæca extend to about the posterior eighth of the body. The testes (Fig. 275, *t.*, *t.*) are in the posterior third and somewhat apart; the anterior one is roundish, the posterior one lobate. The ovary (Fig. 275, *ov.*) is placed at about the middle of the body. The uterus (Fig. 275, *ut.*) appears to be poorly developed, its convolutions spreading laterally barely beyond the cæca.

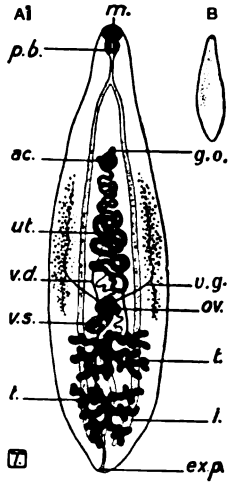


Fig. 274. — Clonorchis sinensis. (*Partly after Looss.*)

A, Magnified; B, natural size.

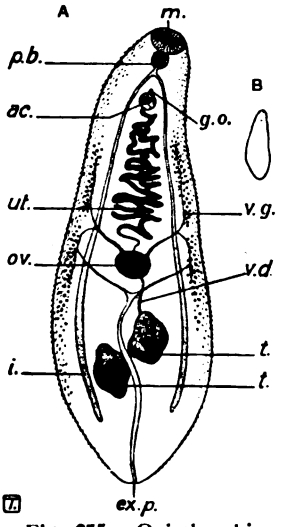


Fig. 275.—Opisthorchis noverca.

A, Greatly magnified; B, natural size. (*See* text.)

(*See* nomenclature on p. 788, footnote.)

The vitelline glands (Fig. 275, *v.g.*) apparently extend from acetabulum to posterior testicle. The eggs are oval and measure 34 μ by 19 to 21 μ (Fig. 181, *f*, p. 655). Nothing is known about its pathogenicity.

Opisthorchis felineus (Rivolta, 1885)

Synonyms.—*Distoma felineum; D. sibericum.*

History and geographical distribution.—Known for long as a parasite of dogs and cats in Europe, *D. felineus* was first found in man by Winogradow in Siberia, and was recognized by Braun as the species commonly found in Annam and in the Philippines. It is not pathogenic to man, although heavy infestations, 200 or more individuals, have been found in the liver and bile-ducts.

The parasite.—*O. felineus* measures 8–11 mm. in length by 1·5–2 mm.

Digitized by Google

in breadth. The cuticle is smooth; the suckers are of equal size, separated from each other by one-fourth of the body length. The eggs are small, yellowish brown, 0·03 mm. long by 0·012 mm. broad. The development, according to Askanazy and Rindfleisch, takes place in fresh-water molluscs. The ripe cercariæ encyst in fresh-water fish, *Abramis vimba* and *Idus melanotis*. Ciurea has found the cysts measuring 0·34 mm. by 0·24 mm. in the Rumania fishes *Tincta tincta* and *Idus idus*. The infestation is contracted by man through eating raw fish.

Varieties of O. felineus. *Opisthorchis viverrini*.—Leiper received from Kerr in Siam a fluke, found in man, differing slightly from *O. felineus*. The cuticle is covered with circular spinelets; the ovary is multilobate: the branches of the gut proceed almost to the posterior end of the body. It is a parasite of the civet cat.

Dicrocœlium dendriticum (Rudolphi, 1819)

Synonyms. — *Fasciola lanceolata; Dicrocœlium lanceatum*, Stiles and Hassall, 1896.

History.—*D. dendriticum* was found by Buchholz in the gall-bladder of man in Germany, and has since been noted in Egypt and Italy. It is found commonly in bile-ducts of animals, especially herbivora, in Europe, Africa, and America.

The parasite (Fig. 276).—A small fluke, 8–10 mm. in length by 1·5–2·51 mm. in breadth. It is attenuated anteriorly, and the widest point is just posterior to the yolk-glands. The intestine bifurcates just in front of the genital pore. The testes lie behind the ventral sucker. The ovary lies behind the posterior testis; there is a receptaculum seminis, also a Laurer's canal. The yolk-glands lie in the lateral portion of the middle fifth of the body. The eggs are thick-shelled, yellowish-brown in colour, measure 38–45 μ by 22–30 μ, and contain an oval miracidium, the anterior end of which is ciliated and provided with a boring spine (Fig. 181, *i*, p. 655). The embryo also possesses a rudimentary intestinal sac.

Life-history.—The larval stages of *D. dendriticum* are passed in the snail *Planorbis marginatus*.

Heterophyes heterophyes (Bilharz and v. Siebold, 1852)

Synonyms.—*Distomum heterophyes; Dicrocœlium heterophyes; Distoma heterophyes; Heterophyes ægyptiaca; Mesogonimus heterophyes; Cœnogonimus heterophyes; Cotylogonimus heterophyes.*

History.—*H. heterophyes* was discovered in 1851 in Cairo by Bilharz at the post-mortem of a child.

Geographical distribution.—It has been reported from Egypt, China, and Japan, and probably has a wide distribution.

Zoological distribution.—Looss has found it in Egypt in the dog (*Canis familiaris*), in the cat (*Felis domesticus*), in a fox (*Canis niloticus*), and in a kite (*Milvus parasiticus*). Janson reports it from the intestine of the dog in Japan, and Yokagawa in Formosa.

The parasite (Fig. 277).—The smallest trematode inhabiting man, excepting *Metagonimus yokagawai*. It measures 1–1·7 mm. in length by 0·3–0·7 mm. in breadth. It has an oval, elongate shape and a reddish colour. The neck is not sharply defined from the body, and may be greatly outstretched. The oral sucker (0·09 mm. in diameter) is subterminal and about one-third the size of the ventral sucker (0·23 mm.), which is placed at about the middle of the body. The cuticle is thickly set with quadrate scales, 5–6 μ long by

Digitized by Google

4 μ broad. The prepharynx is short (80 μ in length); the pharynx measures 50–70 μ in length by 40–50 μ in diameter. The œsophagus is about three times as long. The intestinal cæca extend to the posterior extremity, where they converge and terminate close to the excretory bladder. The lateral ends of the vitelline glands extend beyond the intestinal cæca. The genital pore opens postero-laterally to, and in the immediate vicinity of, the ventral sucker; it is surrounded by a muscular ring. Testicles oval, in extreme posterior end of body. Ovary globular, median and anterior to the testes. Receptaculum seminis as large as the ovary; uterine coils not numerous, and extending between the ventral suckers and the testicles. Eggs light brown, thick-shelled, oval, 20 to 30 μ by 15 to 17 μ; contain a ciliated embryo when oviposited (Fig. 181, *d*, p. 655).

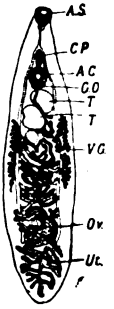


Fig. 276.—Dicrocœlium dendriticum. × 5. (*After Looss.*)

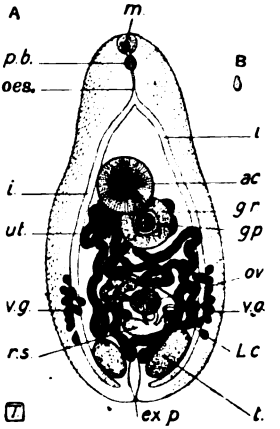


Fig. 277*.—Heterophyes heterophyes.
A, Greatly magnified. B, natural size.

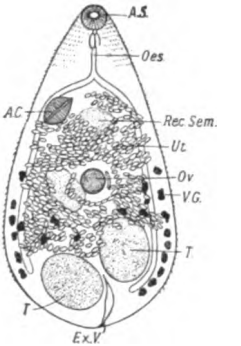


Fig. 278.—Metagonimus yokagawai. × 30. (*After Leiper.*)

The life-history of the parasite is not yet determined. It seems to have little pathological importance, but, according to Low, may cause diarrhœa and dysenteric symptoms. It inhabits the small intestine.

Metagonimus yokagawai (Katsurada, 1912)

Synonyms.—*Tocotrema yokagawa; Heterophyes yokagawa; Yokagawa yokagawa.*

Distribution and life-history.—This parasite (Fig. 278) has been found by Yokagawa to be widely spread among natives of Korea, Formosa, and Japan, in whom it occurs in the intestinal tract. It is believed hitherto to have escaped notice from the resemblance of the egg to that of Clonorchis, and the very small size of the adult. This parasite is common in dogs in China, and belongs to the genus *Metagonimus*, characterized by the arrangement of the yolk-glands and the position of the genital pore, which is situated as a minute slit in the anterior aspect of the ventral sucker: in other

* In addition to nomenclature on page 788: *g.r.*, muscular ring surrounding *g.p.* (genital pore); *L.c.*, Laurer's canal; *ex.v.*, excretory vesicle.

Digitized by Google

respects it resembles the genus *Heterophyes*. There are two intermediary hosts, a fresh-water snail, and a fresh-water fish, as in the case of *C. sinensis*. Muto has traced the redial and cercarial stage in the snail *Melania libertina*, 2·5 per cent. of which he has found to be naturally infested in Japan. The cercaria has two eyespots, an oral and ventral sucker, a simple tail, and a mouth guarded by four to six spines; the body measures 0·2296 mm., the tail 0·286 mm. On emerging from the first intermediary the cercariæ encyst under the scales and in the tissues of the base of the tail and fins of the goldfish and the ayu (*Plecoglossus altivelis*)—often eaten in a raw state by Japanese. The situation of the cercariæ in the fish would indicate that infestation does not take place by the alimentary route in this intermediary host. Mice and dogs can be infected. Yokagawa has shown that the cercariæ can withstand the action of the gastric juice, but that the hyaline capsule is dissolved by its action. The larvæ thus set free develop in the duodenum; they are said to be richly studded with pigment granules. Development is very rapid, and the adult stage is reached in seven to ten days after infestation.

M. yokagawai is only 1·1 mm. long by 0·42–0·7 mm. broad, and is covered with small spines; in the general disposition of its organs it resembles heterophyes; it is much the smallest fluke hitherto found in man. The egg resembles that of *C. sinensis* in size, but is regularly elliptical in shape, dark brown in colour, with a crescent-shaped operculum; the shell membrane has a double contour, and measures 0·033 mm. in length by 0·021 mm. in breadth. *M. yokagawai* is apparently an innocuous parasite in man, causing at most a catarrhal condition of the intestinal canal which it inhabits.

Thymol and naphthol are efficient anthelmintics.

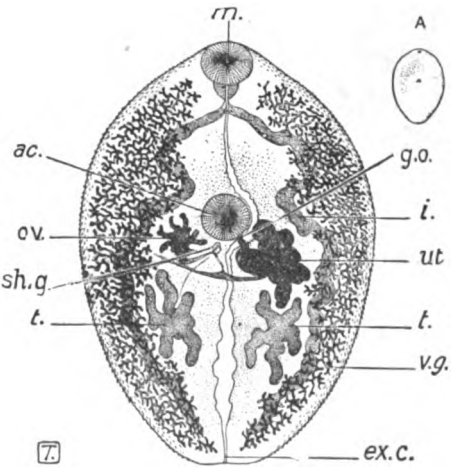


Fig. 279.—**Paragonimus westermanni.** (*Partly after Looss.*)

A, nat. size. (*See* nomenclature on p. 788, footnote.)

PARAGONIMUS WESTERMANNI (Kerbert, 1878)

Synonyms.—*Distoma westermanni; D. ringeri; D. pulmonale; D. cerebrale; Mesogonimus westermanni; M. pulmonalis; M. ringeri.*

Geographical distribution.—*P. westermanni* is confined to China, Japan, Korea, Formosa, and the Philippines.

The parasite (Fig. 279).—*P. westermanni* is reddish-brown in colour, thick and fleshy, and oval in form. So thick is it that its transverse section is almost round. It measures 8–20 mm. in length by 5–9 mm. in breadth, and is covered with broad scale-like spines. The anterior extremity is bluntly rounded and without cephalic cone; the oral sucker (Fig. 279, *m*) (0·88–1·12 by 0·80–0·83 mm.) terminal or subterminal; ventral sucker (Fig. 279, *ac.*) (0·88–1·2 by 0·86–1·44 mm.) slightly larger than the oral sucker and situated

Digitized by Google

somewhat anteriorly to the middle of the body. The pharynx is elongate, but the œsophagus is very short, so that the bifurcation of the intestine is considerably anterior to the ventral sucker. The intestinal cæca (Fig. 279, *i.*) run somewhat zigzag to the caudal end of the body. The genital pore opens close to the posterior margin of the ventral sucker. The testes (Fig. 279, *t.*, *t.*) are tubular, ramified, and situated on each side of the middle line, one slightly posterior to the other. The ovary (Fig. 279, *or.*) is branched and is placed somewhat posteriorly to the ventral sucker, and either to the right or the left of the middle line. The shell-gland is lobate, the uterus (Fig. 279, *ut.*) short and usually massed; the vitellaria (Fig. 279, *v.g.*) are marginal and greatly developed. Laurer's canal is present.

Life-history.—For many years the mode in which this parasite entered man was unknown. Analogy suggested that the ova expectorated by the

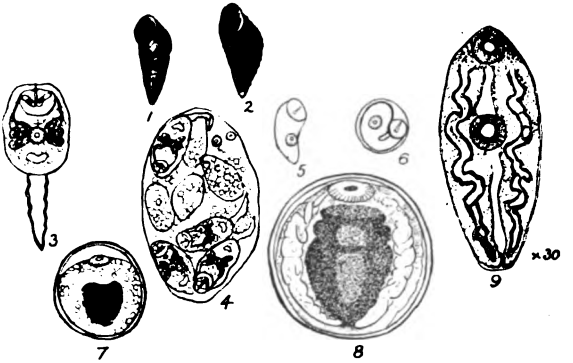


Fig. 280.—Life-history of Paragonimus westermanni. Figs. 3–9, × 15. (*After Nakagawa; "Journ. Exp. Med.," by permission.*)

1, 2, First intermediary hosts, Melania libertina and M. obliquegranulosa, quarter nat. size; 3, 4, cercaria and sporocyst of P. westermanni in Melania; 5, 6, tailless cercaria and encysted cercaria in liver of crab as second intermediary host; 8, fully-grown encysted cercaria; 9, adolescent paragonimus, 14 days old.

host were washed into water—rivers, ponds, wells, etc.—and that the miracidium, on being hatched out, entered some undetected mollusc; but, further than this, conjecture could not venture until Nakagawa, Kakami, Miyairi, Yoshida, Kobayashi, and other Japanese investigators showed that on escape from the egg the miracidium enters a fresh-water snail—various species of the genus Melania, of which at least six have been found to serve as intermediary hosts (*M. libertina*, *obliquegranulosa*, *paucicincta*, and *gottschei*)—wherein it undergoes the usual developmental changes of sporocyst and redia, eventuating in the formation of cercariæ (Fig. 280). The cercariæ in due time escape into the water, and, finding their way into certain species of fresh-water crabs (Figs. 281, 282)—*Potamon obtusipes*, *Sesarma dehaani*, *Eriocheir japonicus*, *E. sinensis*, and *Potamon dehaani*, and also, it would appear, the crayfish (*Astacus japonicus*)—encyst themselves in the liver, muscles, etc., and especially in the gills, and there undergo developmental changes. The rate of infestation of these crustaceans differs in different localities; the numbers of cercarial cysts in a single individual may be as high as

Digitized by Google

1,000; much seems to depend upon the age of the crab and the length of exposure to infection (Kobayashi). The encysted cercariæ are 0·2 mm. in diameter; they possess a conspicuously large excretory vesicle, comparatively large oral and ventral suckers furnished with spines, and no distinguishable alimentary tract (Fig. 280). When introduced into cats the encysted larvæ are able to develop with great rapidity, whether placed in the alimentary

Fig. 281.—Potamon (Geotalphusa) dehaani. Half nat. size

canal or directly in the abdominal cavity. They reach the thoracic organs in ninety-six hours, and hæmoptysis is noted after eight days. The cercariæ, it would appear, on reaching the ileum of man, escape from their cysts in from twenty-four to forty-two hours, penetrate the gut wall and pass into the peritoneal cavity, and a few of them, traversing the diaphragm, enter the

Fig. 282.—Eriocheir japonicus, ♂. Quarter nat. size. (*Partly after Alcock.*)

lungs; a few pass into the liver, muscles, and other organs and tissues, and, after about ninety days, having attained sexual maturity, produce eggs. It is still doubtful as to how the encysted cercaria escapes from the crab, and as to how it obtains, in nature, access to man. However the infection may be acquired in Japan, where raw fish is often eaten, neither the Koreans nor the Formosans eat uncooked crabs, and yet *P. westermanni* is very common

Digitized by Google

in certain districts of Korea and Formosa. Possibly encystment in the crab is not a biological necessity for the parasite; it may be that the cercariæ, which can penetrate the cuticle or organs of the crab, can also penetrate those

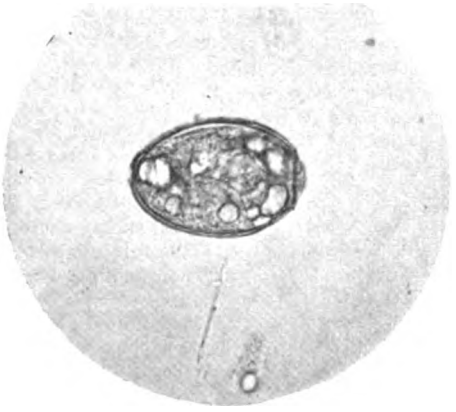


Fig. 283.—Ovum of Paragonimus westermanni. × 250 diam.
(*Microphoto: Dr. A. Norman.*)

of man, and that man is infected with *P. westermanni* in the same way as he is infected with the three species of schistosomes—*S. hæmatobium*, *S. mansoni*, and *S. japonicum*.

The pathogenesis is fully detailed at p. 647.

The ovum (Fig. 283) is ovoid in shape, brown in colour, is provided with an operculum and measures 85–100 μ by 50–67 μ in diameter.

Echinostomum ilocanum (Garrison, 1908)

Synonym.—*Fascioletta ilocana.*

This parasite (Fig. 284) was discovered in 1907 by Garrison, who noticed peculiar eggs in the fæces of Philippine prisoners in Manila, and subsequently obtained a small number of trematodes from the intestinal canal. Odhner has transferred it to the genus *Echinostomum*. In length it is 4–6 mm., and in breadth 0·75–1·35 mm. It is attenuated posteriorly. The acetabulum is much larger than the oral sucker. The genital pore opens separately a little behind the half-way point between the pharynx and the acetabulum. Each testis has an anterior and a posterior lobe. The ovary is globular.

Nothing is known about the life-history of the parasite, beyond the fact that a miracidium hatches in about ten days after the eggs have left the host.

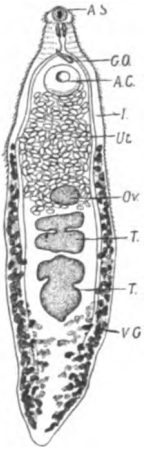


Fig. 284.
Echinostomum ilocanum. ×12 diam.
(*After Odhner.*)
(For nomenclature *see* p. 788, footnote.)

Digitized by Google

ECHINOSTOMUM MALAYANUM (Leiper, 1912)

Synonym.—*Euparyhium malayanum* (Leiper).

Geographical distribution.—Malay States, Siam (Kerr), and Assam (Clayton Lane).

The parasite.—*E. malayanum* is found in the intestines of natives in the Malay States, but probably is not normally parasitic in man. The body is 12 mm. long by 3 mm. in greatest breadth, and 1·3 mm. in thickness; both ends are rounded. There is a row of 43 stout spines of various sizes round the circumoral disc; those on the ventral are 0·07 mm. and those on the dorsal surface 0·05–0·16 mm. in length. The oral sucker comprises one-third of the total diameter of the disc; it communicates with the spheroidal muscular pharynx by a thin-walled portion 0·175 mm. long. The œsophagus measures 0·04 mm. in length, and bifurcates near the pharynx. The main gut branches are simple and end blindly at the posterior end of the body. The ventral sucker, 0·9 by 0·75 mm., is several times larger than the oral. The testes are tandem and are deeply lobed; they are situated in the middle of the body behind the ventral sucker. The cirrus pouch is well developed and extends behind the level of the fundus. The ovary has a smooth surface and lies immediately in front of the anterior testis, 0·85 mm. behind the ventral sucker.

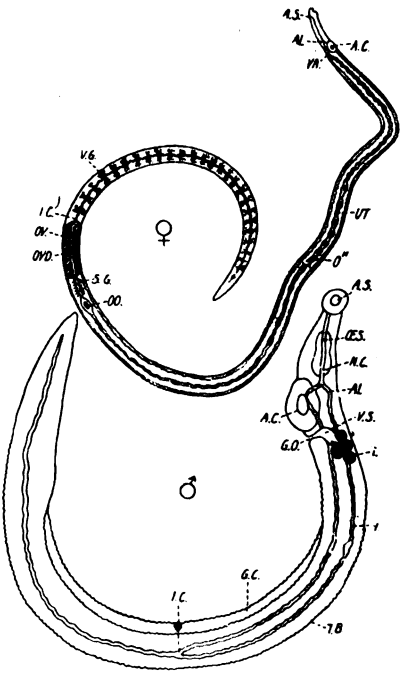


Fig. 285. — Schistosoma hæmatobium. × 20 diam. (*Orig.*)

A.C., Ventral sucker; AL., bifurcation of alimentary canal; A.S., anterior sucker; G.C., gynecophoric canal; G.O., genital opening; I., intestine; I.C., union of intestinal cæca; N.C., nerve cord; o', lateral-spined ovum; o'', terminal-spined ovum; œs., œsophagus; OO., oötype; OV., ovary; OVD., oviduct; S.G., shell-gland; T., testes; T.B., tuberculations; UT., uterus; VA., vagina; V.G., vitelline glands; V.S., vesicula seminalis.

SCHISTOSOMATIDÆ

The general characters and life-history of these parasites have already been detailed (pp. 553–80); the following is a brief summary of the main morphological characteristics :—

SCHISTOSOMA HÆMATOBIUM (Bilharz and v. Siebold, 1852). (Fig. 285.)

Male.—1–1·5 cm. in length. Body behind ventral sucker covered with minute wart-like projections, which are present also on inner margins of the gynæcophoric canal. The alimentary canal bifurcates in front of the ventral sucker to form the intestinal cæca, which pass backwards to the posterior half of the body, where they unite to form a short median tube which terminates

Digitized by Google

blindly near the posterior end of the distome. The genital system consists of 4–5 large, irregularly rounded testes lying behind the ventral sucker, and communicating with the vesicula seminalis by as many vasa efferentia.

Female.—2 cm. in length. The alimentary canal is substantially the same as in the male. The genital system consists of an ovary, an elongated oval organ lying in the posterior half of the body in front of the union of the intestinal cæca, an oviduct which passes forwards to a point anterior to the ovary, where it joins with the vitelline duct and the shell-gland, and the uterus, a long sinuous tube which opens at the genital pore and contains 20–30 terminal-spined ova with their spines directed posteriorly. The ova are 120–150 μ long by 40–60 μ broad, spindle-shaped, with a terminal spine.

The intermediary hosts are fresh-water snails of the genera *Bullinus* and *Physopsis*.

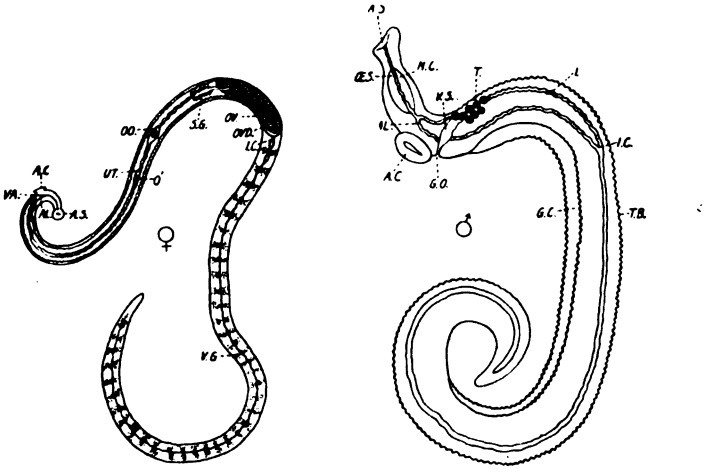


Fig. 286.—Schistosoma mansoni. × 20 diam. (*Orig.*)
(For nomenclature *see* Fig. 285.)

SCHISTOSOMA MANSONI (Sambon, 1907). (Fig. 286.)

Male.—1 cm. long. Body behind the ventral sucker clothed with wart-like tuberculations considerably larger and more pronounced than in *S. hæmatobium*. The intestinal canal bifurcates at the level of the ventral sucker, but the intestinal cæca unite early in the anterior half of the body to form a long, single intestinal tract. The genital system consists of 8–9 small testes, with as many vasa efferentia opening into the vesicula seminalis.

Female.—1·5 cm. in length. As in the male, the intestinal cæca unite in the anterior half of the worm. In the genital system the ovary lies in the anterior half of the body in front of the union of the intestinal cæca, and, in consequence, the uterus is very short and contains a few or, more generally, one lateral-spined ovum with spine directed posteriorly. The yolk-glands occupy about two-thirds of the body at its posterior end. The ova are somewhat shorter than those of *S. hæmatobium*, are provided with a lateral spine, and measure 120 μ by 56 μ.

Intermediary host, fresh-water snails of the genus *Planorbis*.

Digitized by Google

DIFFERENTIAL TABLE OF THE HUMAN SCHISTOSOMES

ADULTS	*S. hæmatobium.*	*S. mansoni.*	*S. japonicum.*
MALE	Length 1·5 cm. Breadth 1 mm. Finely tuberculated. Testes large, four in number, posterior and dorsal to ventral sucker.	Length 1 cm. Breadth 1·2 mm. Grossly tuberculated. Testes small, eight in number, posterior and dorsal to ventral sucker which is generally more prominent.	Length 0·9 cm. Breadth 0·6 mm. Not tuberculated. Testes elliptical in shape, eight in number, posterior and dorsal to ventral sucker.
FEMALE ...	Length 2 cm. Breadth 0·25 mm. Ovary in posterior third in front of intestinal cæca. Uterus contains large numbers of terminal-spined ova. Lateral branches of intestinal canal unite in posterior third. Yolk-glands distributed in posterior fourth of the body.	Length 1·5 cm. Breadth 0·16 mm. Ovary in anterior half of body in front of union of intestinal cæca. Uterus contains one, at most three, lateral-spined ova, with spine directed posteriorly. Yolk-glands widely distributed in posterior half of body.	Length 1·2 cm. Breadth 0·4 mm. Ovary situated in middle of body. Well-developed uterus occupies anterior portion of body and may contain 300 ripe ova. Yolk-glands well developed and occupy posterior half of body.
OVA			
MEASUREMENTS	160 μ long. 40–60 μ broad.	140–150 μ long. 60–70 μ broad.	70–75 μ long. 40–45 μ broad.
SHAPE	Oval or spindle shaped.	Blunt oval.	Rounded.
SPINE	Terminal.	Lateral.	No spine—rudimentary lateral papilla.
PASSAGE TO EXTERIOR	Urine, less frequently fæces.	Fæces, rarely urine.	Fæces only.
CERCARIÆ			(According to Leiper)*
LENGTH OF BODY AND TAIL	About 0·390 mm.	About 0·370 mm.	About 0·25 mm.
BODY	0·19 mm.	0·16 mm.	0·1 mm.
TAIL	0·20 mm.	0·21 mm.	0·1 mm.
FURCA	0·08 mm.	0·06 mm.	0·05 mm.
OUTLINE ON LATERAL VIEW	Marked protrusion of ventral sucker.	No protrusion of ventral sucker.	Ventral sucker slightly protuberant.
SALIVARY-MUCIN GLANDS	Three pairs large acidophil.	Six pairs, two large, four small.	Five pairs, small and granular.
INTERMEDIARY HOST	*Bullinus contortus.* *B. dybowski.* *B. innesi.* *B. forskali ?* *Physopsis africana.*	*Planorbis boissyi.* *P. olivaceus.* *P. guadaloupensis.* *P. centrimetralis.*	*Blanfordia* or *Hypsobia nosophora.*

* Cort and Faust's measurements of this cercaria are considerably bigger than those given by Leiper.

Digitized by Google

SCHISTOSOMA JAPONICUM (Katsurada, 1904). (Fig. 287.)

Male.—9–12 mm. long. Body smooth and non-tuberculated; suckers provided with minute spines. Alimentary canal bifurcates at the level of the ventral sucker and unites posteriorly, the united gut occupying one-quarter to one-fifth of the total body length. The genital system consists of 6–8 oval testes dorsally situated, with a large seminal vesicle.

Female.—12 mm. long. The alimentary canal unites posteriorly as in the male. The ovary is situated in the centre of the body at some distance in front of the union of the intestinal cæca. The yolk-glands are well developed; the uterus is large and occupies the anterior portion of the body, and may contain 50 or more ova. The ova are oval in shape, 60 μ in length and 40 μ in breadth; they possess a rudimentary lateral spine.

Intermediary host, fresh-water snails of the genus *Hypsobia*. For the morphology and differentiation of the cercariæ the reader is referred to the accompanying synoptical table, and to p. 559.

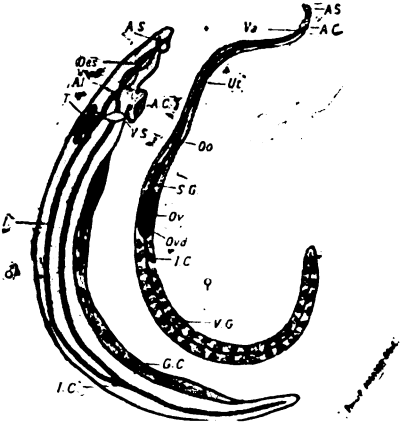


Fig. 287. — Schistosoma japonicum. × 20 diam.
(For nomenclature *see* Fig. 285.)

CERCARIÆ. (Fig. 288.)

Other fork-tailed cercariæ, besides those of the human schistosomes, have been found in snails of the genera *Bullinus*, *Planorbis*, and *Limnæa* in Egypt, India, South Africa, and North America. The majority of these can be differentiated from the schistosome cercariæ of man by their measurements, morphological distinctions, the presence of a pharynx, of eyespots, or by the cuticular expansion of the tail. Some have been found in operculated snails such as Cleopatra and Melania. Therefore the presence of furcocercous cercariæ in fresh-water snails, even of the appropriate genera, does not necessarily indicate the presence of human schistosomiasis in the district.

In India, where the disease is not endemic, fork-tailed cercariæ from *Planorbis exustus* have been found to be intermediary stages of *Schistosoma spindale* of the goat; whilst Sewell has lately described a cercaria, non-pathogenic to man, having apparently a morphology and measurements similar to those of *S. japonicum*, from *P. exustus* and from *Limnæa amygdalum*. The life-history of *S. bovis* is not yet known, and it is possible that certain of the cercariæ depicted in Fig. 124, p. 559, especially those figured by Cawston in *Physopsis africana*, may represent its larval stages.

Many of these furcocercous cercariæ have received different names, such as *Cercaria bilharziella*, *C. oculata*, *C. cercobii*, *C. douthitti*, *C. gladii*, *C. elephantis*, *C. emarginatæ*, *C. douglasi*, and *C. vivax*.

The classification of the many different varieties of cercariæ found in fresh-water snails has been formulated by Lühe as follows:—

Digitized by Google

A, Gasterostome cercariæ. Mouth opening in middle of ventral surface.
B, Monostome cercariæ. Ventral sucker lacking.
C, Amphistome cercariæ. Ventral sucker at posterior end of the body.
D, Lophocercariæ. Longitudinal cuticular projections along each side of the body.

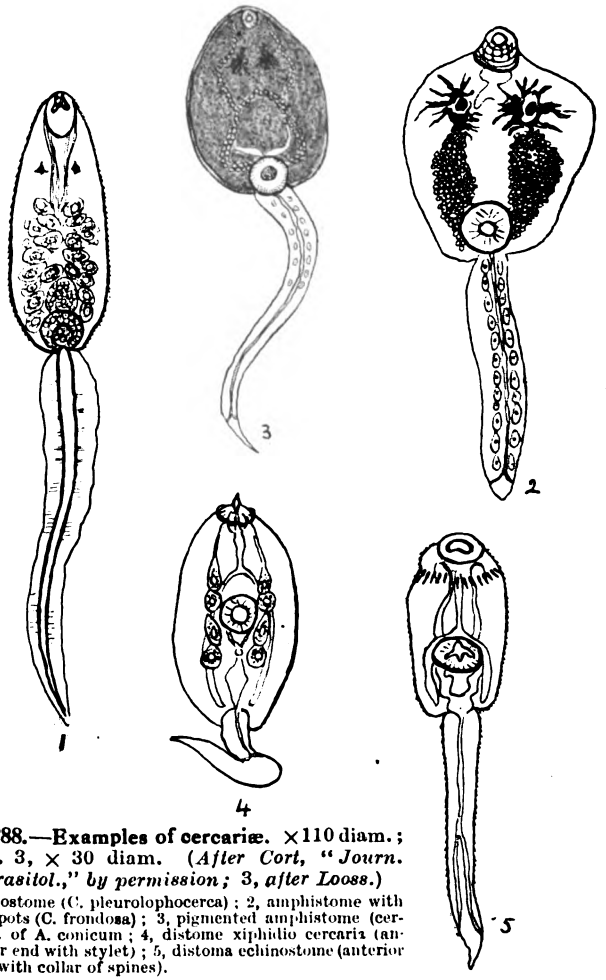


Fig. 288.—Examples of cercariæ. ×110 diam.; No. 3, × 30 diam. (*After Cort, "Journ. Parasitol.," by permission; 3, after Looss.*)

1, Monostome (C. pleurolophocerca); 2, amphistome with eyespots (C. frondosa); 3, pigmented amphistome (cercaria of A. conicum; 4, distome xiphidio cercaria (anterior end with stylet); 5, distoma echinostome (anterior end with collar of spines).

E, Distome cercariæ. Ventral sucker situated towards the middle of body. This class contains many subdivisions, including the *leptocercous cercariæ*, with straight, slender tails; the *microcercous*, with stumpy tails; the *echinostome*, with a circlet of spines surrounding the anterior sucker; and the *furcocercous*, or fork-tailed cercariæ, as detailed on p. 801.

Digitized by Google

WATSONIUS WATSONI (Conyngham, 1904; Stiles and Goldberger, 1910)

Synonyms.—*Amphistomum watsoni*; *Cladorchis watsoni*; *Paramphistomum watsoni*.

History.—This parasite was found in 1904 by Watson in the duodenum and upper part of the jejunum of a negro patient from German West Africa who died of starvation and diarrhœa. The stools, which were numerous, watery, and of a bilious colour, contained many yellow, translucent, oval trematodes. At the post-mortem the jejunum was found to be full of these trematodes, some of them alive and still adherent. The mucosa showed no hæmorrhages, but appeared to be slightly congested. The other parts of the bowel, as also the other organs, were normal. The parasite is said to occur in monkeys and to be common in natives near Lake Tchad, and to be a normal intestinal parasite of monkeys.

The parasite.—*W. watsoni* (Fig. 289) is of a reddish-brown colour and measures 8 to 10 mm. in length by 4 to 5 mm. in breadth; it is oval in shape. The oral sucker is small; the ventral sucker or acetabulum large and at the posterior extremity of the body. The genital pore opens at the anterior end of the ventral surface on a level with the bifurcation of the intestine. The ova measure 125 μ in length by 75 μ in breadth.

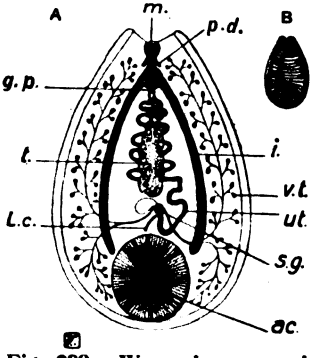


Fig. 289.—Watsonius watsoni. (*After Shipley.*)

A, Magnified; B, natural size.
p.d., Pharyngeal diverticula.
(For nomenclature, *see* Fig. 285.)

Life-history.—We know nothing of the life-history of this parasite, but probably it is similar to that of *Paramphistomum cervi*, the conical fluke of cattle and sheep, which was thoroughly worked out by Looss in 1896. The eggs of *P. cervi* contain a ciliated embryo (miracidium) which escapes from the egg-shell under the stimulus of light and moisture. Swimming about in water, which it must necessarily reach for further development, it penetrates into the visceral cavity of a certain snail (*Bullinus contortus*), and in this develops and multiplies by sporocyst formation. In about two months, having attained the so-called cercaria stage, its progeny escape from the snail, swim around in the water, and finally encyst themselves on plants or other objects. The final host (cattle, sheep, etc.) is attained either through drinking-water or pasture.

Geographical distribution.—Information is as yet very scanty, but there is reason to believe that *W. watsoni* is by no means uncommon in certain parts of Northern Nigeria, where it gives rise to serious intestinal trouble, especially in children. A patient who had lived there for some time told Manson that on one occasion, being seized with violent diarrhœa, he passed about a pint of material containing innumerable moving bodies which he described as resembling the heads of tadpoles—doubtless specimens of *W. watsoni*.

Treatment.—As for adult tapeworms.

Digitized by Google

GASTRODISCOIDES HOMINIS (Leiper, 1913)

Synonyms.—*Amphistomum hominis; Gastrodiscus hominis* (Lewis and McConnell, 1876).

History.—This parasite, described by Lewis and McConnell in 1876, was procured from Assam, from post-mortem material. *G. hominis* is now found to be a much more common parasite of man than was formerly supposed. Leiper on anatomical grounds has included it in the genus Gastrodiscoides on account of the prominent genital papillæ in place of the genital atrium which characterizes the genus Gastrodiscus.

Geographical distribution.—We know little of the geographical distribution of *G. hominis;* it is probably widely distributed throughout Asia, and appears to be rather common in India. The pig, apparently, is its normal host (Mathis and Leger).

The parasite (Fig. 290) is of a reddish colour in fresh specimens, and measures 5–8 mm. in length by 3–4 mm. in breadth. Its body is divided into an anterior, rather slender, conical portion and a posterior, flattened ventrally concave, disc; the oral sucker is small, ventral; the acetabulum is at the posterior border of the ventral disc. The genital pore opens at about the middle of the anterior portion on a level with the bifurcation of the intestine. The testicles are two in number and lobate; the vas deferens is very sinuous. The eggs are oval, measure 150 μ by 72 μ, and are operculated. The life-history has not been worked out, but, arguing from analogy, it is the same as for *Gastrodiscus ægyptiacus* and *Amphistomum conicum*, whose redial and cercarial stages are passed in the digestive gland of various fresh-water snails of the genera *Bullinus, Planorbis,* and *Physa.*

Fig. 290.—Gastrodiscoides hominis. Nat. size.

Pathogenesis.—*G. hominis* is found in the cæcum and colon. The mucous membrane is stippled with numerous red spots resembling leech-bites. These spots are caused by the parasites, which, attaching themselves to the mucosa by means of their suckers, produce minute pimple-like elevations of the surface. When the parasites occur in great numbers they cause much irritation.

Treatment.—The same as for adult tapeworms and ankylostomes—thymol, etc. As many as 200 worms were passed under this treatment in Mackie's case.

CLASS III.—THE CESTODA

The tapeworms are elongated and, as a rule, segmented Platyhelminthes of a white or yellow colour, devoid of mouth or of alimentary canal, but with organs for attachment to the body of their host situated at the anterior extremity. The segments are known as *proglottides,* and a knob-like structure at the anterior extremity is known as the *scolex;* this in turn is separated from the proglottides by a narrow unsegmented portion known as the neck. The scolex itself is provided with organs of adhesion in the shape of suckers and circular rows of hooks which are arranged upon a cylindrical projection known as the *rostellum.* The proglottides increase in size gradually as they are situated farther away from the neck; the most distal are the most mature, the more proximal the more immature segments of the colonial animal, or *strobila.* Each of the older proglottides shows one or more genital openings surrounded by thick lips, openings which vary in position in different species

Digitized by Google

The interior of each proglottis is filled with parenchyma tissue, in which the organs lie, and in which also calcareous bodies, spherical in shape, are embedded.

The *nervous system* consists of a nerve-ring in the anterior part near the scolex, and from this longitudinal cords run through the whole body parallel to the margins of the proglottides, and giving off branches to the various structures in each segment.

The *excretory system* consists of a network of branched canals, originating in each instance from a flame cell. Longitudinal excretory canals run through the whole strobila parallel to the nerves.

The *reproductive system* is formed only in the older and more mature segments. Each mature segment is hermaphrodite and contains both male and female organs. The *male organs* consist of numerous small spherical testes scattered throughout the parenchyma. From each testis there arises a small duct which unites with others to form a vas deferens opening to the exterior by the common genital pore; at its terminal portion the coiled vas lies in the cirrus sac, which can be protruded as a penis and is provided with hooklets or spines. The *female organs* consist of a lobed ovary and a yolk-gland of similar shape lying in close proximity. The oviduct is joined by the vitelline duct, and leads from it into a tubular uterus, which may or may not be branched, and opens to the exterior at the genital opening by means of a tubular vagina of varying length. The shell-glands are situated in the vicinity of the oviduct. The terminal portion of the vagina is hollowed out to form a receptaculum seminis.

Life-history.—The cestodes live normally in the alimentary canal of their host, and especially the small intestine, absorbing their nutriment by osmosis.

The male glands ripen first, and the spermatozoa pass into the vagina of the same or of the neighbouring proglottis. The ovum from the ovary, thus fertilized, is provided with yolk and egg-shell from the glands specialized for the purpose, and passes into the uterus and its diverticula, which in this manner gradually become packed with eggs. The proglottis, when gravid, becomes detached and passes to the exterior with the stool. The eggs are circular, yellow or brown in colour, though in the Dibothriocephalidæ they are oval and provided with an operculum. On reaching water, the egg gives rise to a ciliated *onchosphere*, provided with three pairs of embryonal hooks. This onchosphere, or embryo, cannot develop further unless taken up by an intermediary mammalian or invertebrate host either during eating or drinking. On entering the digestive canal of this host the inner egg-shell or *embryophore* is digested away, and the onchosphere, thus set free, works its way by means of its hooks into the blood-vessels and is carried by the bloodstream to those organs of its host most suited for its further development; there it comes to rest and loses its embryonal hooklets. As a result of the irritation which it sets up in the organs of its intermediary host, a fibrous stroma, known as the *capsule*, soon envelops it.

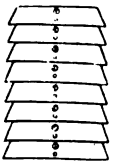
The formation of the larva from the embryo may take place in various ways:

1. The *plerocercoid*, a solid mass, tape-like, with an invaginated scolex.

2. The *cysticercus*, a bladder-like structure filled with fluid in which the scolices arise by proliferation from the walls of the cavity. It is known as a *cysticercoid* when bladder-formation is slight and the larva is provided with a tail; or *cysticercus proper* when the bladder is well developed and the tail absent. Of this latter form three sub-varieties are described: (*a*)

Digitized by Google

CLASSIFICATION OF THE CESTODES PARASITIC IN MAN

GROUP	CHARACTERS	GENUS	EXAMPLE
TÆNIIDÆ Head with four suckers, and it may be one or more rings of hooks. No external uterine opening on each proglottis.	Genital pores alternating on each proglottis. Uterus uninterrupted. Tænia.	*Tænia.* *Cœnurus.* A larval form found in man.	*T. solium.* *T. saginata.* *T. echinococcus.* *C. glomeratus.*
	Genital pores unilateral. Uterus uninterrupted. Hymenolepis.	*Hymenolepis.*	*H. nana.* *H. diminuta.*
	Genital pores unilateral. Uterus contains egg balls.	*Davainea.*	*D. madagascarensis.*
	Two genital pores to each segment. Two sets of genitalia to each segment. Dipylidium.	*Dipylidium.*	*D. caninum.*
DIBOTHRIOCEPHALIDÆ Head without hooks or suckers, but provided with two longitudinal grooves, known as *bothria*. There are one or two uterine openings on each proglottis. The male and female genital openings are separate and lie in the median line.	One row of genital pores situated in the median line.  Dibothriocephalus.	*Dibothriocephalus.*	*D. latus.* *D. mansoni.* Plerocercoid in man, known as *Sparganum mansoni.*
		(*Sparganum.*) A group name for larval forms of which the adult is uncertain, probably a *Dibothriocephalus.*	*S. proliferum.*
	Two rows of genital pores laterally placed. Diplogonoporus.	*Diplogonoporus.*	*D. grandis.*

Digitized by Google

cysticercus proper, in which there is only one bladder cavity and one scolex; (*b*) *cœnurus*, in which there is one bladder cavity and many scolices; (*c*) *echinoccocus*, in which daughter-cysts are budded off, each containing many scolices. The larvæ may remain encysted in the tissues of the intermediary host, but do not undergo any further development till transferred to the alimentary tract of the definitive host. The bladder is then digested, but the scolex and neck of the larva, being resistant, pass into the small intestine, where, affixing themselves to the intestinal wall, they become mature in a comparatively short time. (Fig. 291.)

A classification of the Cestodes parasitic in man appears on p. 806.

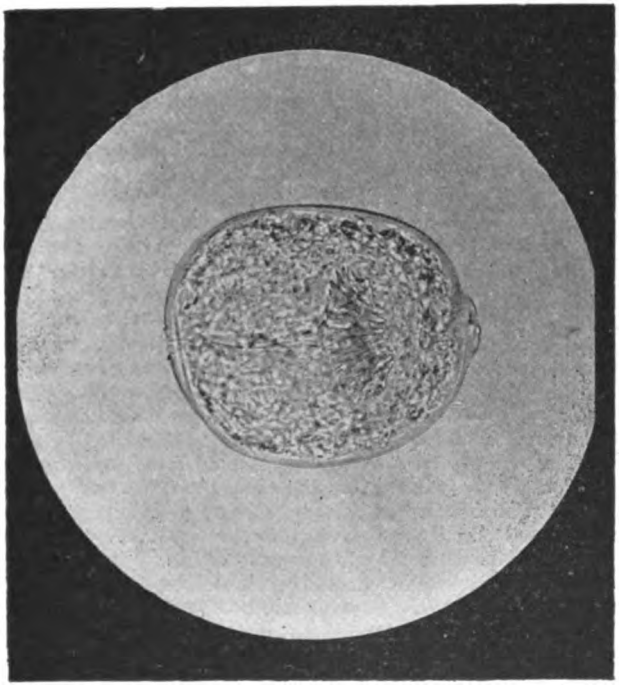


Fig. 291.—Tænia echinococcus cyst. × 70. (*Photo: Dr. J. Bell.*)

TÆNIA SOLIUM, Linn., 1767

Synonyms.—*T. cucurbitina; T. pellucida; T. vulgaris; T. dentata; T. tenella.*

Geographical distribution.—*T. solium* has a worldwide distribution, as coextensive as that of its intermediary host the pig. It is unknown among the Mohammedans and Jews and other races that eschew pork; it is therefore uncommon in Africa and those parts of Asia in which the Mohammedan faith is supreme.

The parasite.—*T. solium* (Fig. 292) is found attached to the anterior third of the small intestine, and generally attains 2–3 metres in length, exceptionally

Digitized by Google

8 metres or more. The head, globular and roughly quadrangular, measures about 1 mm. in diameter. The rostrum is short, slightly pigmented, and bears a double row of 25–50 hooklets. The four suckers project slightly, and are circular in shape, each measuring ¼ mm. in diameter. The anterior proglottides are small, but broader than long; whereas the more mature are just the reverse of this—12 mm. long by 6 mm. broad. Each proglottis bears one marginal genital pore with thick lips; the situation of the pore alternates irregularly between the right and left margins. The uterus lies in the median plane and bears 7–10 stout diverticula. The eggs are globular or slightly oval, 31–56 μ in diameter, and have a vitelline membrane; inside the radially striated shell is a six-hooked onchosphere. (Fig. 182, *a*, p. 655.)

Life-history and pathogenesis.—The mature segments become detached, four or six at a time, and pass to the exterior with the fæces, where, by the process of disintegration, the ova are set free. They are then taken into the alimentary tract of the intermediary host—in this case the pig—either in contaminated water or soiled food, though man himself may exceptionally become infested in the same way. The onchosphere now passes through the gut-wall and, gaining the blood-stream, settles down in the muscular tissue, loses its hooks, and becomes a cysticercus 5–20 mm. long, generally known as *Cysticercus cellulosæ*, in which a small invaginated scolex and neck are produced resembling in miniature the adult tænia. In man, however, the cysticercus may develop in any organ, especially the muscles of the tongue, neck, or ribs; less frequently in the liver, heart, lungs, or brain. A *Cysticercus cellulosæ* has been recorded in the human eye; in one case it is known to have persisted for more than twenty years.

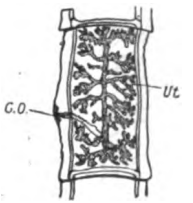


Fig. 292.—Ripe segment of Tænia solium. (*After Brumpt.*)

G.O., Genital opening; Ut., uterus.

Pork-flesh infested with this cysticercus is known as "measly pork."

When the cysticercus is taken into the alimentary tract of man, or the definitive host, the bladder is dissolved by the gastric juices, and the scolex and neck are evaginated; it then passes into the small intestine, where the scolex fixes itself to the gut-wall and proceeds to form proglottides.

The presence of the adult tænia in the intestinal canal of man may be unaccompanied by any symptoms in the healthy adult, but in debilitated individuals or in children it may cause gastro-intestinal disturbances, anorexia, vomiting, hyperæsthesia of nervous origin, and severe anæmia.

Should the cysticerci encyst in the muscles of man they may impede movement, and if in the tongue may cause paralysis of that organ.

TÆNIA SAGINATA, Goeze, 1872

Synonyms.—*T. solium*, Linn., 1767; *T. cucurbitina*; *T. inermis*; *T. mediocanellata*; *T. lata*.

Geographical distribution.—This worm has a worldwide distribution—is found, in fact, wherever ox-flesh is eaten.

The parasite.—*T. saginata* (Fig. 293) is whitish in colour and semi-transparent; a fully adult example measures 4–10 metres, or even longer; it lives in the upper part of the small intestine. The scolex is pear-shaped or cubical, 1–2 mm. in diameter, with four lateral suckers, but without a rostellum or hooks; the suckers are frequently pigmented. In place of the rostellum

Digitized by Google

there is a sucker-like organ at the apex. The neck is fairly long and about half the width of the scolex. The proglottides gradually elongate as they become older; the gravid ones are three or four times longer than they are broad. The genital pore is single, and marginally placed at the hinder end of each proglottis; in position it alternates irregularly between the right and left margins. There are 20–35 lateral branches on each side of the uterus, and these in turn may actually ramify. The ova are more or less globular, 30–40 μ long, and 20–30 μ in diameter. Each ovum is provided with two shells—the egg-shell proper, thin and transparent, and the embryophore, thick and radially striated, containing the onchosphere, with three pairs of embryonal hooklets. (Fig. 182, *b*, p. 655.)

Life-history and pathogenesis.—The gravid proglottides pass to the exterior either in the fæces or independently by their own movements. Once outside the body they creep into grass or herbage, and there disintegrate. The ova are taken into the alimentary canal of the ox, and the onchospheres are set free and pass into the small intestine. After boring their way through the intestinal wall they are carried to muscles in various parts of the body, more especially the pterygoids, the fatty tissues surrounding the heart, the diaphragm, and the tongue. Here they become cysticerci, as in the analogous *T. solium*, 7·5–9 mm. in length by 5·5 mm. in breadth. The cysticerci can live for eight months or thereabouts in the ox, and can only develop further when ingested by man, the definitive host. When this happens the bladder is digested and the liberated scolex passes into the small intestine and affixes itself by means of its suckers to the gut-wall. It is found that the cysts die when heated to the temperature of 48° C.

In the definitive host the parasite may give rise to few symptoms or may cause a certain degree of anæmia.

Varieties of T. saginata.—Several specimens of human tapeworm have been described from time to time as belonging to new species, but they are now held to be aberrant forms or immature examples of *T. saginata*. In this category are included *T. africana*, described by v. Linstow, from German East Africa, in 1900; *T. hominis*, described by the same helminthologist in 1902, from Asiatic Russia; and *T. philippina*, described by Hare in 1907, from Manila.

TÆNIA ECHINOCOCCUS, v. Siebold, 1853

Synonym.—*Echinococcifer echinococcus.*

The adult worm does not infest man, who in this instance acts as the intermediary, while the dog, wolf, or jackal acts as the definitive host. In these animals the adult tænia occurs in large numbers concealed between the villi of the small intestine.

Geographical distribution.—In Europe hydatid cysts—as the larval stage is known—are common in Iceland; they occur in Asia, especially in Arabia; in Africa, in Algeria, Tunis, Egypt, Abyssinia, and the Cape; in America, in Argentine and Uruguay; in Australia they appear to be of common occurrence in Victoria and Tasmania.

The parasite.—*T. echinococcus* is one of the smallest tapeworms known, 2·5–6 mm. in length. The scolex is minute, 0·3 mm. in diameter, irregularly globular in shape, and is provided at its apex with a projecting rostellum which carries two circular rows of hooks of varying size and number. The neck is short and thick. The proglottides number more than four, of which the terminal one is by far the longest, measuring 5 mm. in length; it is the only one which is sexually mature, and it may contain as many as 800 ova.

Digitized by Google

The genital apertures are marginal, one to each proglottis, and have an alternate arrangement. The testes are spherical and numerous; the cirrus pouch is large and pear-shaped. The uterus, tubular and median in position, has short unbranched lateral diverticula. The ova are slightly ovoidal in shape, 32–36 μ in length and 21–30 μ in breadth. The onchosphere is provided with three pairs of embryonal hooklets.

Life-history and pathogenesis.—The gravid proglottis is evacuated with the fæces of the host, and by disintegration the ova are set free. The larval form can develop in other mammals besides man—chiefly the sheep, ox, pig, camel, goat, and rabbit—and may give rise to severe or, it may be, fatal symptoms. The onchosphere, having passed through the intestinal wall, develops into an hydatid cyst in the liver, lungs, kidney, peritoneum, brain, or genitalia, but occasionally also in other situations, such as the long

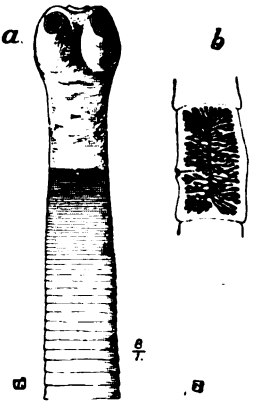


Fig. 293.—Tænia saginata. (*After Braun.*)

a, Cephalic end (magnified); *b*, mature segment (nat. size).

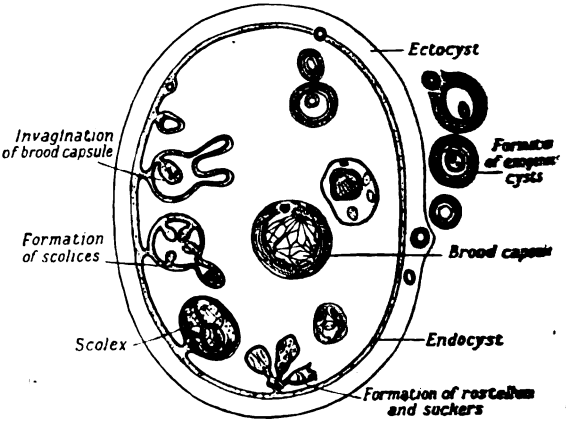


Fig. 294.—Schema of hydatid cyst. (*After Blanchard.*)

bones, the heart, and the orbital cavity. The bladder thus produced may attain the size of a human head; surrounding it there develops a fibrous layer formed from the host's tissues. The cyst-wall itself consists of two layers: (*a*) the ectocyst, a laminated cuticle composed of a chitinous substance; (*b*) the endocyst, a proliferating or germinal layer, which is made up of an outer layer of small cells and an inner layer of larger ones, together with some muscular fibres, calcareous bodies, and glycogen. The bladder itself is filled with a watery fluid composed of inorganic salts, sugar, cholesterin, tyrosin, leucin, and succinic acid. (Fig. 294.)

In man the original cyst may form secondary smaller ones, known as *daughter cysts*, and may proliferate either in an outward direction (exogenous cyst), or inwards towards the cyst cavity (endogenous cyst), and these in turn may produce smaller *granddaughter cysts*. Inside these cysts, by the process of invagination of the germinal layer, *brood-capsules* form, and in the wall of these capsules the larval scolices arise, each provided with a rostellum and hooklets. Many scolices may form inside the one brood-capsule,

Digitized by Google

which, when mature, ruptures and sets free the scolices into the fluid of the mother cyst.

Dogs and jackals become infested with the adult parasite by eating the various organs in which hydatids occur. The cyst-wall becomes digested and the young tæniæ escape into the small intestine in the customary manner.

Man becomes infested by too close association with the usual definitive host the sheepdog. The ova are ingested by using the same dishes as these animals, by kissing infested dogs, and it is also possible that houseflies may disseminate the eggs from the fæces of these animals. Persons of all ages are liable to infestation, but the disease known as hydatids is more common in children under 10 years. The symptoms to which hydatids may give rise are very varied, according to the site of the cyst. They may include symptoms of toxæmia, such as pyrexia, urticaria, and multiform cutaneous eruptions. On the other hand, the fully-developed cyst may appear as a tumour, especially on the liver, and this, on bursting, forms secondary cysts in other organs, or may suppurate and cause general peritonitis. In the brain, hydatids give rise to symptoms of cerebral tumour; while those of the liver, spleen, and peritoneum are liable to simulate malignant growths. Hydatids of the lung give rise to symptoms of compression with the formation of fluid in the pleural cavity. The kidney may be converted into a mass resembling hydronephrosis.

Diagnosis.—The peculiar cystic swelling may possess peculiar physical signs. If it is situated near the surface a fluctuation, known as the "hydatid thrill," may be elicited, but if it is deeply seated this is of little value. On puncture of the cyst with an exploratory syringe the scolices and hooklets may be recognized under the microscope.

Two aids to diagnosis have been described: (1) The precipitin reaction (Welch and Chapman), in which equal parts of preserved hydatid fluid and serum of the suspected case are mingled, the mixture then being incubated for one hour at 37° C. Should the case be infested a precipitate forms; but one should note that this reaction may be exceptionally given by normal serum. (2) The complement-deviation reaction of Weinberg and Parvu, for which the generally-accepted Wassermann technique is employed, using hydatid fluid (0·4 c.c.) as the antigen.

Cœnurus glomeratus, Küchenmeister, 1854

A cœnurus cyst was discovered in the intercostal muscles of a native in Northern Nigeria by Johnson, and was described by Leiper in 1919. The cyst measured 2 cm. by 1 cm.; the wall was very delicate and transparent. Projecting into the cavity of the cyst were 35 buds or invaginated scolices packed with calcareous bodies. The suckers measured 130 μ in diameter and bore 32 hooks, 16 large and as many smaller ones. These hooks can be recognized by their possessing a short, conical handle and a well-curved blade. (Fig. 295.) The largest are 90–110 μ, the smallest 65–70 μ—measurements similar to those obtained by Raillict and Henry in *C. glomeratus* from the gerbil.

Fig. 295.—Hooks of Cœnurus glomeratus. (*After Leiper.*)

Hymenolepis nana (v. Siebold, 1852)

Synonyms.—*Tænia nana; Diplacanthus nanus; Hymenolepis murina.*

History.—This minutest of the tapeworms inhabiting man was first found as a human parasite by Bilharz, in Cairo, in 1851. Grassi thought it

Digitized by Google

was identical with *H. murina* of the rat, but neither he nor, later, Looss has succeeded in tracing its development in that rodent. It is probable that, as in *H. murina*, the parasite can dispense with an intermediary host, and can penetrate into a villus of the intestine and become a cysticercoid, and can then re-enter the canal to become transformed into the adult.

Zoological distribution.—*H. nana* is found in the brown rat (*Rattus norvegicus*), black rat (*R. rattus*), house mouse (*M. musculus*), dwarf field-mouse (*M. minutus*), and garden dormouse (*Eliomys quercinus*).

Geographical distribution.—*H. nana* is found in Egypt, the Sudan, Siam, Japan, the southern States of the American Union, Brazil, Argentina, and throughout Europe, but more especially in the warmer parts, as in Sicily, where, according to Calandruccio, 10 per cent. of the children are affected. Over 1,000 have been found at one autopsy.

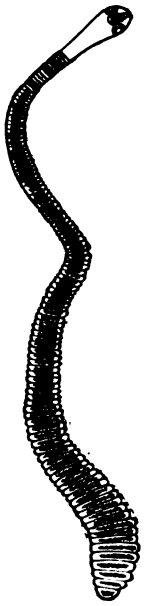


Fig. 296.
Hymenolepis nana.
Magnified.

The parasite (Fig. 296).—The strobila vary in length from 5–45 mm. with the number of proglottides, which may be from about 100 to 200. The scolex is subglobular and measures 139–480 μ in diameter; it is provided with a well-developed rostellum armed with a single crown of 20–30 hooklets 14–18 μ long; the suckers are globular and have a diameter of 80–150 μ. The neck is long. The proglottides are very short anteriorly: farther down the chain they increase in size but remain broader than long. Only the hindermost segments may equal or even slightly exceed their breadth. The maximum breadth of the proglottides is 0·5–0·9 mm. The genital pores open on the margin near the anterior border of each segment. There are three testes in each segment; the vas deferens widens to form a seminal vesicle. The gravid uterus occupies nearly the entire segment. The eggs number 80–180 in each proglottis; they are oval or globular, and present two distinct membranes; the outer one measures from 40–46 μ in diameter, the inner one 20–34 μ. The latter exhibits at each pole a more or less conspicuous mamillate projection, and encloses an onchosphere with three pairs of embryonic hooks. (Fig. 182, *c*, p. 655.)

Development.—The development of *Hymenolepis murina* has been worked out experimentally by Grassi in the rat, and is probably the same as for *H. nana*. The egg is swallowed and, after hatching, enters a villus in the lower part of the small intestine (Fig. 297), where it transforms into a *cercocystis*.* The six-hooked embryo is found encysted 24–50 hours after ingestion, its long axis corresponding to that of the villus, and the posterior end bearing the embryonal hooks directed towards the lumen of the intestine. Occasionally two parasites may be found in the same villus. In about 40–70 hours after ingestion the scolex has appeared, and in 80–90 hours after ingestion the rostellum is provided with hooklets. Then the parasite passes into the lumen of the intestine, where it can be seen attached to the

* The term *cercocystis* was introduced by Villot to designate those cysticercoids which are provided with caudal appendages.

Digitized by Google

epithelium of the villus with short neck and no trace of segmentation. The rapidity of development varies somewhat, and, as a rule, various stages are found occurring simultaneously in the same host. Strobilization is rapid; the proglottides attain maturity in about 10–12 days, and about 30 days after infection the eggs of the parasite begin to appear in the fæces. These never develop in the same host unless reintroduced per os or through a reverse peristalsis, because, as in *Oxyuris vermicularis*, the embryo will not hatch unless the egg be subjected to the action of the gastric juices. Young white rats proved most susceptible to the infection, whilst rats already harbouring the parasites were refractory. Grassi's observations do not entirely disprove the possible agency of an intermediary host as in other tapeworms, but they certainly show that it can be dispensed with, and indeed that, as a rule, the rat acts as both definitive and intermediary host. Experiments in man were not conclusive. Out of eight persons fed with eggs, or mature segments of the parasite both from man and rats, only one became infested. This occurred, however, in a region (Catania) where many harbour this tapeworm.

Pathogenesis.—*H. nana* is very minute, but, as a rule, it occurs in large numbers—usually hundreds, not infrequently thousands. When attached to the intestine it fixes its rostellum deeply into the lumen of a Lieberkühn's follicle, thus altering and destroying many of the epithelial cells. It is obvious, therefore, that a number of these worms must give rise to considerable irritation and possibly favour secondary infection. According to Grassi, *H. nana* may bore deeply into the mucosa; and at the post-mortem of a case in which 400 specimens were found in the ileum, Visconti and Segré noticed that the mucosa throughout the small intestine was tumefied, hyperæmic, and covered with a thick layer of greyish mucus, through which the worms were scattered. The most frequent symptoms reported by authors are abdominal pain, which may, or may not, be associated with diarrhœa; convulsions of various sorts, frequently epileptiform; headache and strabismus. The nervous phenomena are ascribed to the absorption of toxic products elaborated by the parasite. On account of its small size this parasite is easily overlooked. Diagnosis is based on the presence of the characteristic ova in the fæces. Some care is requisite in looking for the eggs, because, owing to their transparency, they may escape observation.

Treatment.—*H. nana* is readily expelled by male fern. If a patient harbours this parasite he should not be allowed to sleep in the same bed with another person. On prophylactic grounds one can surmise that the rat is the intermediary, and therefore these rodents and mice should be banished from the house and all food kept out of their reach.

HYMENOLEPIS DIMINUTA (Rudolphi, 1819)

Synonyms.—*Tænia leptocephala; T. flavopunctata; T. minima.*

Geographical distribution.—*H. diminuta* is a parasite of the rat (*R. decumanus, rattus*, and *alexandrinus*), and has been found in man in Italy, South America, Congo, and West Indies.

The parasite.—The length is 20–30 cm., the breadth 3·5 mm. The head is very small, cuboidal in shape, with a small infundibulum at the apex in which a protractile rostellum is situated; there are four small suckers. The neck is shorter than the head, and the proglottides increase in size but are considerably broader than they are long. The ova are circular or slightly ovoid; the outer shell is yellowish and thickened, with indistinct radiations containing a hexacanth onchosphere.

Digitized by Google

Life-history.—The cysticercus stage takes place in the body cavity of certain insects, especially the rat-fleas (*Ceratophyllus fasciatus*, *Xenopsylla cheopis*), and also certain coleoptera (*Akis spinosa*, *Asopia farinalis*, and *Scaurus striatus*). Man becomes accidentally infested, apparently by eating insufficiently-cooked bread in which these coleoptera occur. The rat itself is said to be easily parasiticized by eating infested fleas.

Davainea madagascariensis (Davaine, 1869)

Synonyms.—*Tænia madagascariensis ; T. demerariensis.*

History.—*D. madagascariensis* was first described by Davaine in 1869. In 1891 Leuckart described an entire specimen with scolex from Siam, but it is chiefly to Blanchard that we owe our knowledge of this parasite.

Geographical distribution.—Ten cases have been recorded, mostly in children ; there is one recorded case in an adult in British Guiana, by

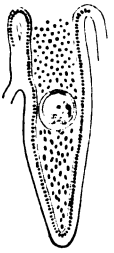


Fig. 297.—Embryo of Hymenolepis nana in small intestine.

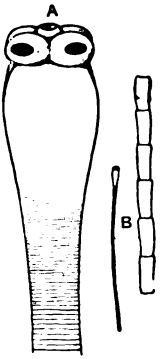


Fig. 298.—Davainea madagascariensis. (*After Blanchard.*)
A, Head (magnified); B, parasite (nat. size).

Fig. 299.—Davainea asiatica : sagittal section of gravid segment. (*After Linstow.*)

Daniels. Cases of this infestation have been noted from Mauritius, Siam, British Guiana, and the Philippines.

Zoological distribution.—As yet *D. madagascariensis* has only been found in man, but the genus is widely distributed in rats, in hares, and in several birds, such as the ostrich, rhea, emu, egret, parrot, partridge, grouse, etc.

The parasite (Fig. 298).—The strobila attains 25–30 cm. in length by 1·4 mm. in breadth, and is composed of 500–600 proglottides. The scolex is provided with four large round suckers and a retractile rostellum surrounded by five concentric rings of hooklets, about 110 in all. The rostellum when invaginated forms a kind of pouch which gives it the appearance of an apical sucker; it is provided with hooks. The proximal segments are broader than long, the distal longer than broad (2 by 1·4 mm.). The last 100 proglottides, resembling apple seeds, are gravid and form one-half the length of the entire strobila. (Fig. 299.) The genital spores are unilateral and

Digitized by Google

open near the proximal corners of the segments. The cirrus pouch is fusiform, the ductus ejaculatorius very long and sinuous, the testes are over 50 in number. The receptaculum seminis is unusually long and broad; it extends to the middle of the segment and communicates with the oviduct. The uterus is composed of a number of tubes rolled up on each side into an almost spherical coil containing 300 or more egg-balls. The globular onchosphere (8 μ to 15 μ) is surrounded by two perfectly transparent shells, the outer one of which bears two pointed projections. The ova measure 99 μ by 46 μ.

Life-history.—The cystic stage of this parasite is unknown. Blanchard suggested that it might be found in cockroaches (*Periplaneta orientalis*, *P. americana*, etc.).

Pathogenesis.—We know nothing of the pathogenesis of this form of tæniasis.

Two other varieties of Davainea have been reported in man—*D. asiatica* by Linstow in 1901, and *D. formosana* by Akashi in 1916—but it is very doubtful whether they can be considered distinct.

Dipylidium caninum (Linn., 1767)

Synonyms.—*T. caninum*; *T. moniliformis*; *T. cucumerina*; *T. elliptica*.

Geographical distribution.—*D. caninum* is a common parasite of dogs, cats, and jackals. In man it has been found, mostly in children, in Germany, Italy, and Spain.

The parasite.—A long cestode, 15–40 cm. in length and of a maximal breadth of 2–3 mm. The scolex is a small and globular point 0·55 mm. in diameter. The rostellum, which can be retracted into an infundibulum, has a single circle consisting of 28–30 small hooklets, each 14–18 μ in length. There are four elliptical suckers. The proglottides are very narrow and number 200 or more; the more mature measure 2–3 mm. in breadth and 6–7 mm. in length, so that they are considerably longer than broad. They are of a reddish colour resembling cucumber seeds. The genital apparatus develops late and only in the most mature segments. The genital pores lie symmetrically at the lateral margins of each segment. The uterine cavities contain egg-sacs, each with 8–15 ova, which are round and measure 35–40 μ in diameter (Fig. 300); the vagina is not provided with a receptaculum seminis. The mature proglottides leave the intestine spontaneously.

As a rule, *D. caninum* infestations produce no untoward symptoms. The larval or cysticercoid stage takes place in the dog-louse (*Trichodectis canis*), in the dog-flea (*Ctenocephalus canis*), or in the human flea (*Pulex irritans*).

Dibothriocephalus latus, Linn., 1748

Synonyms.—*Bothriocephalus latus*; *B. cristatus*; *B. latissimus*.

Geographical distribution.—*D. latus* is a parasite of the small intestine of man, the dog and cat; it is known as the "broad tapeworm." It has a wide distribution in Europe, especially in Sweden, Russia, Switzerland, and Rumania; in Asia it is common in Turkestan and Japan; in Africa, in Madagascar and the Central African lake districts.

The parasite is greyish in colour and it may attain the length of 10 metres. Multiple infestations are not infrequent. The scolex is oblong, about 3 mm. in length, and is unprovided with suckers, rostellum, or hooklets; but extending throughout its length are two longitudinal grooves called *bothria*. The neck is thin and the proglottides number 3,000–4,000. The

Digitized by Google

mature segments are considerably broader than long. The genital apparatus is situated in the median line. The testes are numerous and are situated dorsally; the vas deferens passes anteriorly and forms a seminal vesicle before entering the cirrus pouch. The genital pore is single for each proglottis and median in position. The ovary is bilobed and is also medially placed. The shell-glands lie in a posterior plane, and the uterus forms numerous transverse convolutions while passing forwards to meet the vas deferens.

Life-history and pathogenesis.—The ova (Fig. 182, *d*, p. 655) are operculated, brown, and measure 70 μ in length by 45 μ. The rather complicated life-history of *D. latus* has been worked out by Rosen (1918), and lately confirmed by Galli-Valerio. There are, it appears, two intermediary hosts, a cyclops and certain fresh-water fishes. The egg on coming into

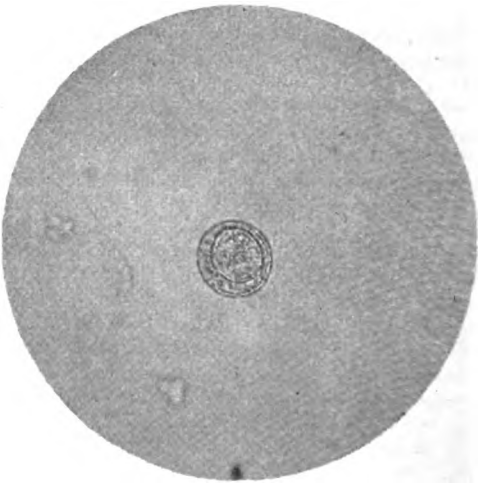


Fig. 300.—Ovum of Dipylidium caninum. × 250 diam.
(*Microphoto: Dr. J. Bell.*)

contact with water gives exit to a *coracidium*, that is a ciliated *onchosphere* contained within an embryonic envelope. After an interval of three or four days the *onchosphere* itself, 22–30 μ in diameter, escapes and is ingested by certain fresh-water crustacea—*Cyclops strenuus* and *Diaptomus gracilis*—in the intestinal canal of which it is, within a period of two to three weeks, transformed into a *procercoid larva*—an elongated sphere, finely clothed with hairs, with a terminal spherical appendix, 0·5–0·6 mm. in length. It would appear that, at the most, only two such procercoids can develop in one individual cyclops, from which, when taken into the stomach of fresh-water fishes, the pike, perch, trout, or tench, the larvæ are immediately liberated; they penetrate the stomach wall, and after three or four days appear in the body cavity, and soon become encysted as *plerocercoid larvæ*, 6 mm. in length, in the muscular tissue of these fishes. Here they develop characteristic cephalic grooves, or *bothria*, alimentary, nervous, and excretory systems; and on being ingested with raw or insufficiently-cooked fish the plerocercoid

Digitized by Google

develops into the adult dibothriocephalus in the intestinal canal of man. The symptoms produced by *D. latus* may be trifling; on the other hand, deterioration of blood, producing an anæmia of a severe type, may ensue.

DIBOTHRIOCEPHALUS MANSONI (Cobbold, 1882)

Synonyms.—*Ligula mansoni*; *Bothriocephalus liguloides* (Leuckart, 1886); *B. mansoni*; *Dibothrium mansoni*; *Sparganum mansoni*.

This parasite, the larva of a cestode belonging to the family Dibothriocephalidæ, was relegated provisionally to the artificial collective group Sparganum. It was discovered in 1882 by Manson in making the post-mortem examination of a Chinaman in Amoy. Since that date 55 cases have been reported. From feeding experiments with laboratory-bred dogs, Yoshida considered it to be the larval stage of *Dibothriocephalus mansoni*.

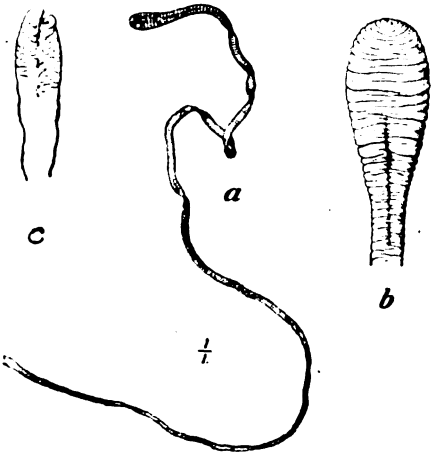


Fig. 301.—Sparganum mansoni. (*After Sambon.*)

a, Natural size; *b*, anterior extremity; *c*, posterior extremity. Extracted from an abscess in a Masai.

This discovery has been confirmed by Okumura, who has found that the adult dibothriocephalus is a parasite of the intestine of the dog and cat. The ova, after 3–7 weeks' incubation in water, hatch out into ciliated onchospheres; they then enter a cyclops (*C. leuckartii*), in whose body cavity they become transformed after 21 days into "procercoids"—elongated structures 0·27 mm. in length by 0·08 mm. in breadth. The cyclops is then ingested by a frog (*Rana nigromaculata*) or a snake (*Elaphe climacophora*), when the larvæ become plerocercoids identical with *Sparganum mansoni*. It would appear that it has long been known that these frogs and snakes harboured plerocercoids indistinguishable from *Sparganum mansoni*. The following measurements of Sparganum have been given: length, 8–36 cm.; breadth, 0·1–12 mm.; thickness, 0·5–1·75 mm. During life the parasites are extremely elastic; after immersion in alcohol they contract and wrinkle. The anterior end is broader than the posterior, is rounded and presents a papilliform projection on which is found the compressed and more or less completely invaginated head. (Fig. 301.) The body is flat, unsegmented, and trans-

Digitized by Google

versely wrinkled. On the ventral surface there is, as a rule, a distinct longitudinal median groove; on the dorsal surface there may be two longitudinal grooves. No sexual organs are present.

In Manson's original case the parasites (11) lay under the peritoneum in the neighbourhood of the kidneys and iliac fossæ, and (1) apparently free in the pleural cavity. They were more or less coiled up and irregularly disposed in the subperitoneal fascia, looking like ribbon-strings of fat until turned out, when they exhibited feeble yet distinct movements. Scheube found a specimen in the urethra of a Japanese. Ijima and Murata, in a study of 10 cases in Japan and China, also found the same parasite in the urethra; the worm appearing during micturition with its head projecting from the urethra and occluding it. In 1918 a similar instance was recorded by Cleland from Australia, in which a worm 10 cm. long was passed per urethram. Thrice very young specimens have been found in Japan, lying beneath the conjunctiva and producing swellings the size of a bean. In one of the Japanese cases the parasite was found in the subcutaneous connective tissue of the thigh, where during nine years it gave rise to indolent tumours that recurred fairly regularly every summer at about the same spot; it seemed to change its position very readily, disappearing in about ten days. At the time of its last appearance the swelling attained the size of a fist; an abscess formed, from which the worm was extracted. A similar parasite, identified by Sambon, was likewise extracted from an abscess on the thigh of a Masai, in German East Africa, by Baxter; and another was found by Daniels in a Carib in British Guiana.

As already mentioned, Sparganum is probably a normal parasite of the cat or dog, and the adult a dibothriocephalus. Looss believed the definitive host to be an aquatic animal (a bird or a fish), because the parasite appears to endeavour to leave the body of its intermediary host, apparently by the urethra, as Scheube suggested.

Ocular sparganosis.—Casaux and others have recently called attention to the marked frequency in and about the Tonkin delta of the condition they designate ocular sparganosis. Pain, redness, œdema of the upper eyelid, with lachrymation and marked ptosis, lead to an examination and the discovery of an almond-sized indurated nodule. Incision of this reveals a small yellowish fatty mass which on section is found to contain a coiled-up *S. mansoni*. It is probable that in these cases similar parasites are present in other regions of the body.

Diplogonoporus grandis (R. Blanchard, 1894)

Synonym.—*Krabbea grandis.*

Diplogonoporus represents a genus of the Dibothriocephalidæ, comparable to *Dipylidium* in the Tæniadæ—that is to say, the genital organs are symmetrically doubled in each segment. It is a parasite of cetaceans and seals; only two cases have been observed in man, both in Japanese. The worm is of great length, 10–25 metres. The ova (Fig. 182, *e*, p. 655) have thick shells, are brown in colour, and measure 63 μ by 48 μ. The life-history is unknown, but probably takes place in a fish.

Sparganum proliferum (Ijima, 1905)

Synonyms.—*Plerocercoides prolifer; Plerocercus prolifer.*

History.—*S. proliferum* has been reported once, in 1905, from Tokyo, Japan. It was found encysted in the subcutaneous tissue in man. A second and almost identical case was reported in 1918 in a fisherman in Florida.

Digitized by Google

According to Ijima, who describes it, this larva (Fig. 302) may attain 1–12 mm. in length by 2·5 mm. in breadth. The anterior is narrower and more motile than the posterior end, and may exhibit an apical depression which possibly serves as a sucker. The body, with the exception of the head, contains a number of roundish calcareous corpuscles, and in older specimens there are also reserve-food bodies irregularly distributed. They give rise to supernumerary heads, which become independent. There are no genital organs.

In the cases reported, thousands of parasites were present. In a small piece of skin, 11 cm., Ijima found as many as 60. The worms occupied small roundish or ovoid cysts (1–8 mm. long by 2–5 mm. in width) in the subcutaneous cellular tissue. The cysts could be enucleated quite easily, and contained one or more parasites. It is thought that they were in the process of division within the cyst-walls, which would explain the large number found within a single cyst. When present for years they caused an enlarged condition of the thigh and an acne-like appearance of the skin.

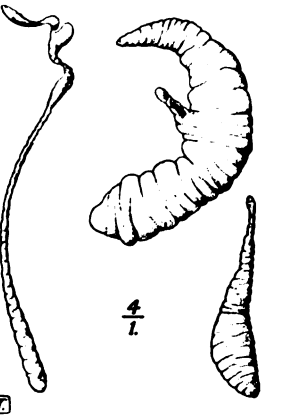


Fig. 302.—Different forms of Sparganum proliferum. (*After Ijima.*)

Nothing further is at present known of the life-history of the parasite, though by analogy it is thought to be the larval stage of a bothriocephaloid worm.

PHYLUM NEMATHELMINTHES

The Nemathelminthes are bilaterally symmetrical animals, generally cylindrical in shape, and for the most part parasitic in vertebrates and invertebrates. There is a well-developed muscular layer, generally consisting of longitudinal fibres; a body cavity is always present. The Nemathelminthes are divisible into three classes:

Class I. Nematoda.
„ II. Gordiaciæ.
„ III. Acanthocephala.

Class I.—THE NEMATODA

The nematodes are cylindrical non-segmented worms, usually tapering at both ends; in colour they are white or yellow, sometimes semi-transparent.

The *alimentary canal* is complete from mouth to anus, which is subterminal.

The *nervous system*, when present, consists of an œsophageal ring from which a variable number of nerve filaments run in a posterior direction.

The *excretory system* consists of two longitudinal vessels, which unite anteriorly and open on the ventral surface in the median line by an excretory pore.

The genital organs.—The sexes are generally separated; the *male* being smaller than the female and distinguished by a curved or twisted tail, or a

Digitized by Google

cuticular expansion—or bursa—adapted for copulatory purposes. The male organs consist of a long coiled tube, the anterior portion representing the testis; the centre, the vas deferens; while the terminal portion functions as the vesicula seminalis. The ductus ejaculatorius with glandular walls terminates near the rectum. The cloaca accommodates one or two chitinous rods, or spicules, which lie in a muscular sac; these organs facilitate the entrance of the spermatozoa into the female vagina.

The *female* organs consist generally of two coiled tubes. The upper or glandular portion of each tube represents the ovary; the middle, the oviduct; and the terminal functions as the uterus. At the junction of the uteri there is a dilatation or a receptaculum seminis. The two uteri join to form a short median vagina, which opens in the mid-ventral line of the anterior half of the body. The upper portion of the uterus is glandular and represents the shell-gland. The uteri are generally distended with ova already fertilized.

Passing along the whole length of the body there run four longitudinal lines dividing the body itself into four equal parts. The body wall consists of a chitinous skin or cuticle investing the whole body, and a muscular layer composed of longitudinal fibres.

These worms possess a body cavity filled with amœboid cells in which the organs lie.

Life-history.—The egg consists of a shell containing a fertilized cell and numerous yolk-granules. The egg develops further by one of two processes known as *direct* and *indirect*. In no case are sexually mature worms produced from fertilized eggs in the host in which the parasites exist.

Direct development.—This may take place in four different ways:

1. The eggs leave the body in an unsegmented condition and develop in damp ground. When the embryo inside the egg-shell is ripe, it is ingested by its new host. Example, *Trichuris*.

2. The eggs leave the body in a fully segmented condition and may be taken up immediately by the new host. Example, *Oxyuris*.

3. The eggs leave the body in a partly segmented condition and develop into a larva outside the body in the fæces and earth, and when mature enter their new host by boring through the skin. Examples, *Ankylostoma* and *Necator*.

4. The eggs develop on the ground into larvæ which become sexually mature, and, after copulation has taken place, the now fertilized female in turn lays eggs; these hatch into other larvæ, not sexually differentiated, which themselves re-enter man by boring through the tissues. Example, *Strongyloides stercoralis*.

Indirect development.—This may take place in three ways:

1. The female nematode in the intestinal canal is viviparous, and the larvæ must enter an intermediary host in order to complete development. In the latter animal they enter the tissues; here they become mature and encyst. Further development is only possible if the tissues of the intermediary host are eaten by the definitive host. Example, *Trichinella spiralis*.

2. The viviparous female nematode situated in the connective or lymphatic tissues produces active embryos which circulate in the blood and are taken up by blood-sucking insects acting as intermediaries. Example, *Filaria bancrofti*.

3. The viviparous female lives in the connective tissues underneath the skin and voids active embryos into water, where they enter into a fresh-water crustacean—which, in this instance, acts as the intermediary host—and are again ingested by man. Example, *Dracunculus medinensis*.

Digitized by Google

CLASSIFICATION OF THE NEMATODES PARASITIC IN MAN

GROUP	CHARACTERS	GENUS	EXAMPLE
ASCARIDÆ	Massive body; mouth provided with three muscular lips.	*Ascaris.* *Lagochilascaris.*	*A. lumbricoides.* *L. minor.*
STRONGYLIDÆ	Mouth provided with six papillæ and often with a chitinous armature. Male generally provided with a copulatory bursa.	*Oxyuris.* *Eustrongylus.* *Trichostrongylus.* *Hæmonchus.* *Œsophagostomum.* *Ternidens.* *Ankylostoma.* ,, *Necator.* *Physaloptera.* *Syngamus.*	*O. vermicularis.* *E. visceralis.* *T. instabilis.* *H. contortus.* *O. apiostomum.* *T. deminutus.* *A. duodenale.* *A. ceylanicum.* *N. americanus.* *P. mordens.* *S. kingi.*
TRICHOTRACHELIDÆ	The anterior half of the body filiform, containing the œsophagus.	*Trichuris.* *Trichinella.*	*T. trichiura.* *T. spiralis.*
FILARIIDÆ	Body cylindrical and narrow. Development in an intermediary host.	*Filaria.* ,, ,, *Dirofilaria.* *Loa.* *Thelazia.* *Acanthocheilonema.* *Onchocerca.*	*F. bancrofti.* *F. ozzardi.* *F. conjunctivæ.* *D. magalhaesi.* *L. loa.* *T. callipæda.* *A. perstans.* *O. volvulus.*
	Unprovided with an anus.	*Dracunculus.*	*D. medinensis.*
GNATHOSTOMIDÆ ...	Mouth provided with two lips; body incompletely clothed with chitinous plates.	*Gnathostomum.*	*G. spinigerum.*
ANGIOSTOMIDÆ ...	Small cylindrical worms undergoing a heterogonous cycle outside the body.	*Strongyloides.*	*S. stercoralis.*

ASCARIS LUMBRICOIDES (Linn., 1758)

Geographical distribution.—Though not quite so common as Trichuris in tropical countries, Ascaris is nevertheless very common indeed, especially in children, who often harbour these loathsome creatures in dozens or even hundreds. Outside the tropics this worm has a wide distribution.

The parasite.—The female measures 20–25 cm., the male 15–17 cm. In colour they are pale yellow or brown, with whitish longitudinal lines; in shape they are round, and taper at both ends. The mouth opens at the anterior end and is guarded by thin lips with finely denticulated margins. The anus is subterminal. In the male the tail is curved in a semicircle, the lips are well provided with papillæ, and there are two chitinous spicules.

Digitized by Google

The eggs are elliptical, 50–75 μ in length by 40–50 μ in breadth, and are encased in a rough albuminous coat, more or less intensely stained by the fæcal pigments; this gives them a mamillated appearance.

Life-history.—The reason for the great frequency of *Ascaris lumbricoides* in tropical countries is probably twofold—the warmth of the climate, and the habits of the people with regard to the disposal of night-soil. In the fæces the ova of this parasite exhibit no trace of segmentation or of differentiated embryo; but if placed in water, or kept moist and in a warm place, in the course of one or more months—longer or shorter according to temperature—the larva is developed, and can be seen coiled up and moving about inside the egg-shell. Formerly it was held that, if such an egg is accidentally or intentionally swallowed, on arrival in the stomach the shell is dissolved away and the contained larva is set free. In a month it grows into a sexually mature animal, and, if both sexes are present, eggs in countless numbers are soon produced and appear in the fæces. Desiccation of the egg at atmospheric temperature does not destroy the larva, which will quickly revive on becoming moistened. In many warm countries night-soil is the favourite fertilizer, and is regularly collected and spread upon the fields. In this way the ova of the ascaris obtain an opportunity of maturing, and thus, too, they have an opportunity of being swallowed by man. They may also be washed into drinking-water; or, becoming desiccated on the drying-up of the fields, be blown about as dust; or they may become attached to fruit or vegetable. In one of these or in similar ways they finally reach the human stomach and there attain maturity.

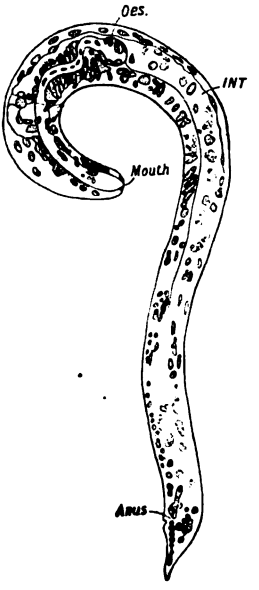


Fig. 303. — Developing form of Ascaris lumbricoides. × 45 diam. (*After Stewart, "Parasitology," by permission.*)

INT = intestine.

This view of the life-history of *A. lumbricoides* was based on numerous experiments on man by Continental observers, and until recently seemed to be justified. Stewart, however, has shown that if ripe ascaris ova are fed to mice and certain other rodents, the larvæ, or a proportion of them, on being hatched out, bore their way into the liver and lungs. In the latter organs they appear in about a week's time, and, if the dose of eggs has been a large one, may cause fatal pneumonia. In experiments made on sucking-pigs, this investigator found that exactly the same process takes place as in rats and mice: for instance, he has found the larvæ abundant in the lungs and trachea on the eighth day; on the ninth they begin to travel down the alimentary canal, and on the following day appear in considerable numbers in the fæces, especially in the colon and cæcum. They measure 1·3–2 mm. on the tenth day, and 1·75–2·37 mm. on the fifteenth. (Fig. 303.) Later observations by Yoshida, Ransom and Foster have confirmed this work on guinea-pigs, rabbits, goats, sheep, and monkeys, while the experiments of Mosler and Lutz indicate that the same process takes place in man. The transition from

Digitized by Google

the larva in the lungs to the adult in the intestine has not yet been fully traced. These experiments certainly show that the larval ascaris leaves the lumen of the gut, and explain the purpose of the beak-like organ with which its cephalic end is furnished. It is more than possible that full development can take place in one host only; on the other hand, Stewart and Yoshida have shown that larvæ taken from the body of one animal can infect another—an occurrence only likely to take place in nature in carnivorous animals.

For pathogenesis *see* p. 657. There is reason to believe that a considerable amount of the debility of natives in the tropics is due to this parasite.

Fig. 304.—Lagochilascaris minor, ♂. × 11 diam. (*After Leiper.*)

LAGOCHILASCARIS MINOR (Leiper, 1909)

This species (Fig. 304) is normally an intestinal parasite, and its occurrence under the skin of man undoubtedly indicates an abnormal infection. A single example was removed from an abscess in a native of Trinidad. The male is 9 mm. by 0·2 mm., the female 15 mm. in length. There are three cuticular lips, separated from the body by a cuticular ring. A narrow keel-like edge of cuticle extends along both sides of the body. The two spicules are solid chitinous rods. The preanal papillæ number over 24 pairs; there are at least 5 pairs of postanal papillæ. The ova have clear, thick shells and measure 65 μ in diameter.

L. minor is a near relative of *L. major* of the lion.

OXYURIS VERMICULARIS (Linn., 1767)

Synonym.—*Fusuria vermicularis.*

Geographical distribution.—This is world-wide.

The parasite.—The habitat of *O. vermicularis* (Fig. 305) is in the upper part of the large intestine, especially the cæcum. Immature forms inhabit the small intestine. The adults are small, transparent, and white in colour; anteriorly they are expanded. The mouth is provided with thin retractile lips; laterally on each side are placed two longitudinal crests. (Fig. 306.) The capacious œsophagus is provided with a bulb. The male measures 2–5 mm. in length, with the posterior extremity curved in a spiral manner and provided with a single hook-like spicule 70 μ in length. The female is

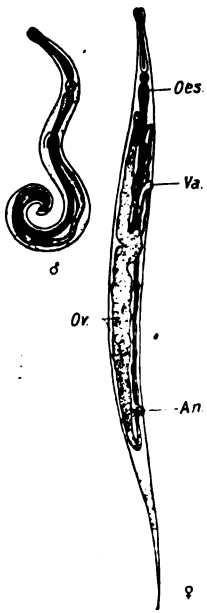


Fig. 305.—Oxyuris vermicularis. × 8 diam. (*After Brumpt.*)

Digitized by Google

considerably longer, 9–12 mm. in length, with a long, pointed tail; the anus is situated about 2 mm. from the posterior extremity; the vulva, transverse and slit-like, is situated in the anterior fourth of the body. The eggs are glossy and unsymmetrical—that is to say, they are flattened on one side. They measure 50–54 μ in length and 20–27 μ in breadth. The egg-shell is thick and colourless, and encloses a transparent non-granular embryo. (Fig. 307.)

Life-history and pathogenesis.—The fertilized females leave the cæcum and travel to the lower part of the large intestine, where their eggs are deposited to find their way to the exterior with the fæces of their host. The gravid females herself may emerge from the anal orifice. When freshly laid the egg contains an almost fully formed embryo which does not complete

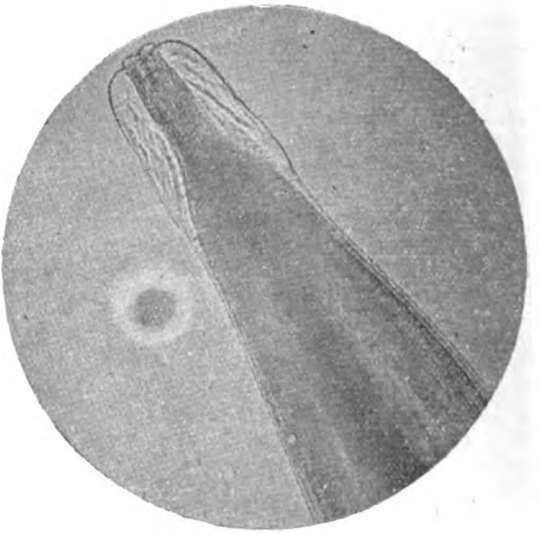


Fig. 306.—Head of Oxyuris vermicularis, showing cuticular expansion. (*Microphoto: Dr. J. Bell.*)

development until taken into the intestinal canal of the new host. When brought into contact with water it dies. The gastric juices dissolve the egg-shell and set free the embryo, which assumes the larval state and travels as such to the appropriate position in the small intestine. In small numbers these worms cause hardly any appreciable symptoms. Generally, as the result of auto-infestation, they occur in very large numbers in the intestinal canal, giving rise to obscure gastro-intestinal symptoms, nervous irritability, and pruritus ani, and may lead to engorgement and excoriation of the neighbouring genital organs from scratching.

It appears that mature oxyurids are capable of penetrating the mucosa and of actually encysting in the submucosa of the small intestine and appendix. In the latter organ they may constitute the primary exciting cause of inflammation. Quite recently (1919 20) infestation of man with the mouse and rat oxyurid *Syphacea obvelata* has been recorded. The ova

Digitized by Google

are twice the length of those of *O. vermicularis*, are more fusiform in shape, and very asymmetrical. They measure 125 μ by 40 μ.

The ova of *S. obvelata* were found by Kofoid and White in 427 cases out of 140,000 soldiers, mostly from the southern United States.

Eustrongylus visceralis (Gmelin, 1789)

Synonyms.—*Eustrongylus gigas ; Strongylus renalis.*

The parasite.—The worms are reddish in colour, cylindrical, and tapering at both extremities. The lateral lines are provided with a series of small punctiform papillæ. The mouth is hexagonal, and surrounded by six nodosities covered with papillæ. The male is 14–40 cm. long by 4–6 mm. broad. The posterior extremity is bursate. There is a single spicule 5–6 mm. in

Fig. 307.—Ovum of Oxyuris vermicularis. × 250 diam.
(*Microphoto : Dr. J. Bell.*)

length. The female measures 20 cm. to 1 metre in length and 5–12 mm. in breadth ; the anus is terminal ; the vulva is situated 50–70 mm. posterior to the mouth. The eggs are elliptical, thick-shelled, brown in colour, and measure 64–68 μ in length by 40–44 μ in breadth.

Pathogenesis.—*E. visceralis* is a parasite of the kidneys of the dog, wolf, polecat, and several mammals, including the seal, in all of which it may cause renal symptoms of considerable gravity.

The worm, which at first occupies the pelvis, may eventually destroy the whole renal substance. There are several recorded instances of infestation in man, with passage of sanguino-purulent urine, and renal pain of the most acute character.

Trichostrongylus instabilis (Railliet, 1893)

Synonym.—*Strongylus subtilis* (Looss, 1895).

Looss has described a very delicate nematode (Figs. 308-10) frequently

Digitized by Google

encountered in Egyptian fellaheen, and since found by Ijima in Japan. Its habitat is at the upper part of the small intestine. The male, which is provided with two spicules, is 4–5 mm. in length by 0·07 mm. in breadth; the female is slightly larger and is much more abundant than the male. The eggs (Fig. 179, *a*, p. 654) are oval, thin-shelled, with an unsegmented vitellus,

Fig. 308.—Trichostrongylus instabilis, male.

and measure 63 μ by 41 μ. This parasite does not occur in large numbers; and, as its mouth is unarmed and its dimensions are exceedingly minute, it does not appear calculated to give rise to any particular symptoms.

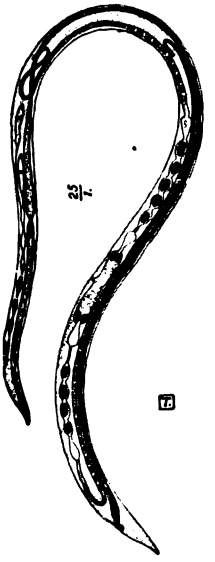


Fig. 309.—T. instabilis, female.

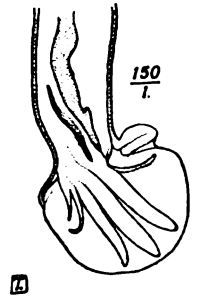


Fig. 310.—T. instabilis: bursa. (*After Looss.*)

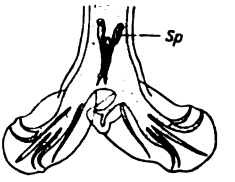


Fig. 311.—Bursa of Hæmonchus contortus. (*After Brumpt.*)
Sp., spicule.

HÆMONCHUS CONTORTUS (Rudolphi, 1803)

This is an intestinal parasite of the goat, sheep, and ox, in which it produces a kind of pernicious anæmia. It has once been found as an intestinal infestation in man by Magalhaes in Brazil.

Digitized by Google

The parasite.—*H. contortus* is a filiform worm attenuated at both extremities; at some little distance from the head two small, laterally-placed papillæ are situated. The integument is finely striated in a transverse direction. The mouth is simple. The male is 10–20 mm. in length, the posterior extremity being expanded into a bilobed bursa, of which the right lobe is provided with a lateral expansion; there are two spicules—0·3–0·5 mm. in length—and an oval accessory piece. (Fig. 311.) The female is 20–30 mm. in length, with a narrow, finely pointed tail. The vagina is situated in the posterior fifth of the body. The eggs are elliptical in shape, and measure 70–95 μ in length and 43–54 μ in breadth. The rhabditiform embryos hatch in water and undergo several moults, after which infestation occurs directly by ingestion.

ŒSOPHAGOSTOMUM APIOSTOMUM, Willach, 1891

Synonym.—*Œ. brumpti*, Railliet and Henry, 1905.

History.—The occurrence in man of this parasitic nematode was discovered by Brumpt, in 1902, at the post-mortem of a negro on the river Omo, Africa. Six immature females were found within cyst-like nodules in the wall of the cæcum and colon. Subsequently the same parasite was found by Leiper in natives from Northern Nigeria. Johnson found that 4 per cent. of the prisoners in Zungeru Jail were infected with the same helminth. We know already of a number of species of the same genus occurring in the Quadrumana. *Œ. apiostomum* has been found in the gorilla, in the orang-outang, in the chimpanzee, and in various monkeys belonging to the genera *Cercopithecus*, *Cynocephalus*, and *Macacus*; in these, if the infection is severe, it gives rise to dysenteric symptoms.

Fig. 312. **Bursa of Œsophagostomum apiostomum, ♂.** (*After Brumpt.*)

The parasite.—The young females found by Brumpt varied in length from 8·5 to 10·5 mm., and presented a maximum breadth of 295 μ to 325 μ. The cuticle is transversely striated; anteriorly it exhibits the ovoid cuticular expansion characteristic of the genus, limited in front by a salient oral ring (*oral vestibule*), and posteriorly by a constriction which is especially marked on the ventral surface, 200 μ distant from the oral vestibule. Posteriorly the female worm tapers gradually to a caudal point slightly bent dorsally. The male has a terminal bursa similar to that of the *Ankylostoma duodenale*, but differs in that the trunk of the dorsal ray bifurcates, some distance from the bursal edge, into two branches forming a horseshoe-shaped structure, each limb of which gives off a short lateral horn near its base. The oral vestibule is provided with a crown of twelve sharp chitinous plates directed forwards and inwards, and bears six papillæ, two lateral and four submedian. The œsophagus is club-shaped and measures 470–500 μ in length by 150 μ in its widest diameter. Anteriorly, owing to its resemblance to *Ascaris lumbricoides* it has been mistaken for miniature specimens of the latter. The males are 50 mm., the females 55 mm. in length, and 2–3 mm. in breadth. The posterior end tapers rapidly in the female, terminating in a sharp point. The mouth has a cuticular cuff and two lips provided with papillæ and teeth. The bursa is bladder-shaped with pedunculated external papillæ and unequal spicules. (Fig. 312.) The female has two ovaries, the vulva being situated anteriorly.

Digitized by Google

TERNIDENS DEMINUTUS (Railliet and Henry, 1905)

Synonym.—*Triodontophorus deminutus*, Railliet and Henry, 1905.

This sclerostome (Fig. 313) is an intestinal parasite inhabiting the large intestine of monkeys. It has several times been found in natives post

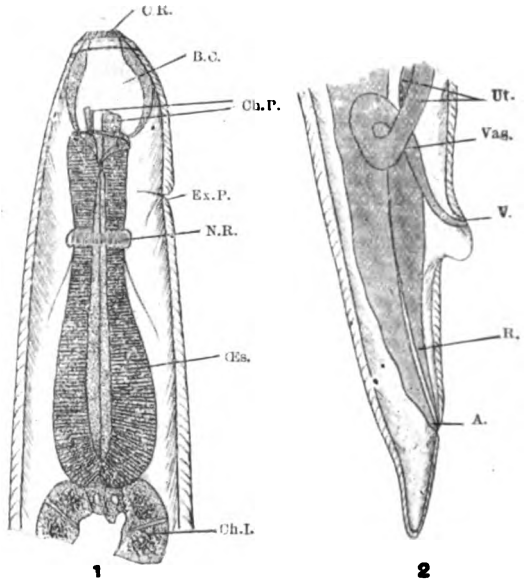


Fig. 313.—Ternidens deminutus, female. (*After Leiper.*)

1, Anterior extremity. 2, Posterior extremity. C.R., corona radiata; B.C., buccal cavity; Ch.P., chitinous plates; N., nerve ring; Œs., œsophagus; Ch.I., chyle intest.; Ut., uterus; Vag., vagina; V., vaginal opening; R., rectum; A., anus.

mortem, by Turner in the Transvaal and by Stannus in Nyasaland. The worms are about the size and shape of a female ankylostome. The male is 9·5 mm. long and 0·56 mm. broad, the female 14–16 mm. in length and 0·73 mm. broad. The male has a terminal bursa provided with a posterior ray split into two widely arching component parts, vaguely recalling the arrangement in œsophagostomum, and is apt to be mistaken for the ankylostoma. (Fig. 314.) The female has a long, tapering extremity. The genital orifice opens posteriorly. The vagina is short and opens into two uterine tubes. The mouth collar is moderately developed, and the entrance to the mouth is surrounded by a double series of delicate fringes composed of cuticle—the *corona radiata*. The buccal capsule is a barrel-shaped chitinous structure; posteriorly it comes into contact with the œsophagus. The œsophagus is stout and muscular and triradiate on section. Each of the surfaces of the œsophagus terminates in a chitinous plate projecting into the buccal capsule. The cuticle is transversely striated.

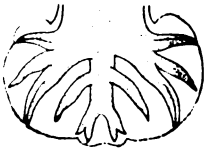


Fig. 314.—Bursa of Ternidens deminutus, ♂. (*After Brumpt.*)

Digitized by Google

ANKYLOSTOMA DUODENALE, Dubini, 1843

Synonyms.—*Strongylus duodenalis; Dochmius duodenalis; Uncinaria duodenalis.*

The parasite.—This ankylostome is an intestinal parasite of man only.

The *male* measures 8–11 mm. in length by 0·4–0·5 mm. in breadth. The tail is expanded into a trilobed bursa (Fig. 315) with eleven ribs, and has two long and very delicate spicules. The greater part of the body is occupied by the genital organs, a much-coiled testis leading into a vesicula seminalis and an elongated ejaculatory duct. The genital opening is posterior in the centre of the cloaca.

The *female* measures 10–13 mm. in length by 0·6 mm. in breadth. The body is cylindrical and slightly expanded posteriorly. The vagina is situated in the posterior third of the body. The greater part of the body cavity is occupied by the ovary and much-coiled uterine tubes containing characteristic ova.

There are two well-marked cephalic glands, which occupy the anterior third of the body in both sexes. The anterior part is occupied by the buccal capsule, in which four strong hooks are placed, two on each side of the ventral and two on each side of the dorsal line. The eggs, elliptical in shape, with a transparent shell, measure 60 μ in length by 40 μ in breadth. When freshly deposited they contain two to four blastomeres each. In damp soil a rhabditiform embryo hatches out, which, after several moults, re-enters man by boring through the skin.

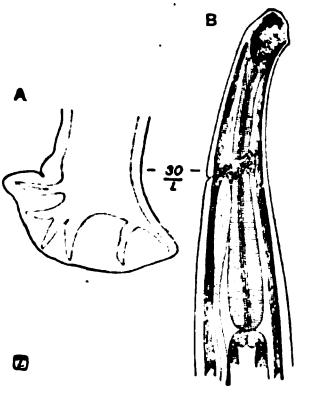


Fig. 315.—Ankylostoma duodenale, male. (*After Looss.*)
A, Bursa; B, head.

ANKYLOSTOMA CEYLANICUM, Looss, 1911

Synonym.—*Ankylostomum braziliense*, Faria, 1910.

A. ceylanicum is a parasite of the civet cat in Ceylon, and has been found in African lions born in Calcutta. According to Leiper, it is identical with *A. braziliense* of dogs and cats in Brazil. It has been found by Clayton Lane in the stools of three prisoners in Mymensing Jail in India, and by Kerr in 12 per cent. of prisoners in Siam. The male is 5 mm. long and is provided with a lobed bursa having clefts dividing the dorsal from the lateral lobes, the rays of which are multiradiate. (Fig. 316.) The female is smaller than *A. duodenale*, 7 mm. long, but resembles that worm in other respects, except that in both sexes the mouth capsule is provided with two pairs of ventral marginal teeth.

NECATOR AMERICANUS (W. Stiles, 1902)

Synonyms.—*Uncinaria americana; Anchylostomum americanum*, Verdun, 1907.

History and geographical distribution.—This species was discovered by Stiles in cases of ankylostomiasis in America, though its range is by no means confined to the New World, as its name would seem to indicate. It has been found southwards from Virginia to Brazil, in Central and West Africa, in India, Ceylon, the Pacific islands, and Philippines. Probably it is as widely

Digitized by Google

diffused as *A. duodenale ;* in Fiji and Ceylon, for example, it is the commonest ankylostome encountered.

The parasite.—*N. americanus* is a shorter and more slender worm than *A. duodenale.* (Fig. 319.)

The *male* measures 7–9 mm. in length by 0·3 mm. in breadth. The caudal bursa possesses a short dorso-median lobe which appears as if divided into two; the dorsal ray branches at its base into divergent arms with bipartite tips, instead of tridigitate as in *A. duodenale.* The common base of the dorsal and dorso-lateral rays is very short. (Fig. 317.) There are two separate spicules, which unite to form a single terminal prong.

The *female* measures 9–11 mm. in length by 0·4 mm. in breadth. The vulva is placed slightly in front of the middle of the body. Copulation of the sexes, as in *A. duodenale,* takes place at the same Y-shaped angle.

The buccal capsule is also smaller than in that species, and presents an irregular border; in place of four ventral hook-like teeth, it has a ventral

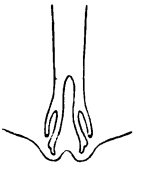


Fig. 316.—Dorsal ray of Ankylostoma ceylanicum. (*After Leiper.*)

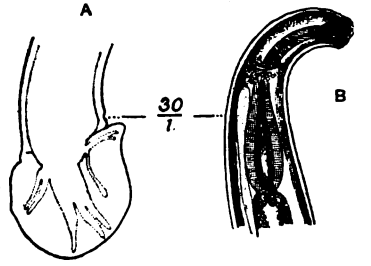


Fig. 317.—Necator americanus. A, Bursa; B, head. (*After Looss.*)

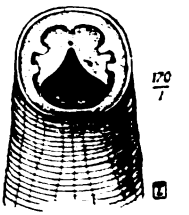


Fig. 318.—Necator americanus, head.

pair of prominent semilunar plates similar to those of the dog ankylostome (*A. stenocephala*); the pair of dorsal teeth is likewise represented by a pair of slightly developed chitinous plates of the same nature. The outlet of the dorsal gland, usually called the dorsal rib or tooth, projects prominently into the oral cavity. Deeply placed in the capsule are one pair of dorsal and one pair of ventral submedian lancets. (Fig. 318.) The eggs are slightly larger than those of *A. duodenale,* and measure 64–75 μ in length by 36–40 μ in breadth.

The following *summary of the life-history of these ankylostome worms* will be found useful:—

Eggs.—Deposited in the human intestine with two, four, or eight blastomeres; on reaching the outer world they give rise in twenty-four hours to—

Rhabditiform larvæ (first stage).—Moult on the third day at 27° C.; on the fifth day the pharyngeal bulbs disappear; moult a second time, then encyst and become—

Encysted strongyloid larvæ (second stage).—These larvæ generally penetrate the skin, but rarely entering by the mouth, and eventually reach the human intestine, where they give rise to—

Digitized by Google

Larvæ without a buccal capsule (third stage).—These moult from the fifth to the seventh day after entry (third moult) and become—

Larvæ with a provisional buccal capsule (fourth stage).—These moult for the fourth time on the fifteenth day after entry, and grow into—

Larvæ with a definite buccal capsule (fifth and last stage).—These grow rapidly in size, and in three or four weeks become *adult male and female worms.*

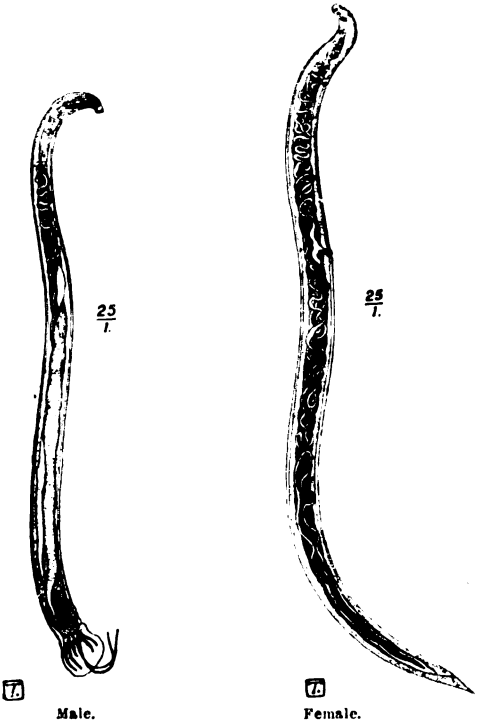


Fig. 319.—Necator americanus. (*After Placencia.*)

PHYSALOPTERA MORDENS, Leiper, 1907

History and geographical distribution.—This worm appears to be a common intestinal parasite in natives of Uganda and Nyasaland, and was originally found by Leiper in material sent by Turner from Portuguese East Africa. The parasites attach themselves to the mucous membrane of the stomach, small intestine, and œsophagus. Superficially they resemble immature *A. lumbricoides* and are apt to be mistaken for them. The monkey is the normal reservoir host.

The parasite.—The male is 30–50 mm. in length and is provided with a bladder-shaped bursa with pedunculated external papillæ and spicules of unequal length. The female measures 40–55 mm. in length and 2–3 mm. in breadth; the posterior end tapers rapidly, terminating in a sharp point.

Digitized by Google

There are two ovaries, a single uterine tube, and the vulva is situated anteriorly. The mouth of physaloptera is of characteristic shape, being cleft-like, situated on the dorso-ventral aspect, provided with a cuticular cuff, and surrounded by stout lips, each of which is armed with papillæ and teeth. (Fig. 320.) The eggs measure 45 μ in length and 35 μ in breadth, and are provided with a thick, smooth shell.

V. Linstow (1902) described a smaller species, found in Southern Russia, as *P. caucasia*.

Syngamus kingi, Leiper, 1913

History.—Specimens of this parasite have been described by Leiper from material supplied by King, of St. Lucia. The worms, in copula, are said to have been coughed up by a woman.

The parasite (Fig. 321).—Copulation is permanent, males and females being found adherent to one another. The measurements of the species have not been given. The male has two unequal spicules in a caudal bursa

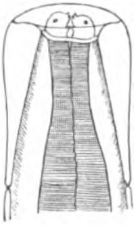


Fig. 320.—Head of Physaloptera mordens. (*After Leiper.*)

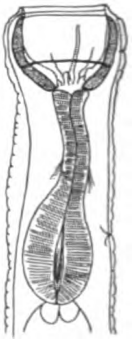


Fig. 321.—Heads of Syngamus kingi. (*After Leiper.*)

provided with many ribs. In both sexes the mouth is large and terminal and leads into a dilated buccal capsule, at the bottom of which are six sharp teeth. Leiper was at first of the opinion that this parasite was related to *S. trachealis* of fowls, but further examination has convinced him that it is probably a new species, allied to *S. dispar* of the puma (*Felis concolor*).

Trichuris trichiura (Linnæus, 1767), Stiles, 1901

Synonyms.—*Ascaris trichiura ; Trichocephalus hominis ; T. dispar.*

Geographical distribution.—The whip-worm (Fig. 322) has a very wide range in temperate countries as well as in the tropics.

The parasite.—The worms are white or, it may be, slightly pink in colour. The male is 40–45 mm. in length, of which the anterior attenuated portion is longer than the posterior, in the proportion of 3 : 2 ; the spicule, which is large and posteriorly situated, is enclosed in a sac-like sheath, which in turn is studded with small serrated spines. The female is 30–35 mm. in length, while the attenuated anterior end is longer than the posterior as 2 : 1. The eggs, of characteristic shape, are brown in colour and measure 50 μ in length and 22 μ in breadth (Fig. 179, *c*, p. 654).

Digitized by Google

Life-history and pathogenesis.—On leaving the body the eggs are unsegmented and the contained embryo develops but slowly, attaining its full length in 6–12 months. Owing to its thick shell it can withstand a low temperature. The embryos can live, without developing any further, apparently, for as long a period as five years. Development is direct; once ingested, the larvæ attain maturity within a month.

The worm lives chiefly in the cæcum. In many countries it is present in more than half the population. It is believed to maintain its position by transfixing, pin-fashion, with its long slender neck, a superficial fold of the mucous membrane. Wichmann claims to have shown, by serial sections of the cæcum at sites where the parasites were fixed, that it is merely embedded in the mucus between the intestinal villi. According to Powell, the females very much preponderate, the proportion to males being as 466 to 1. Except

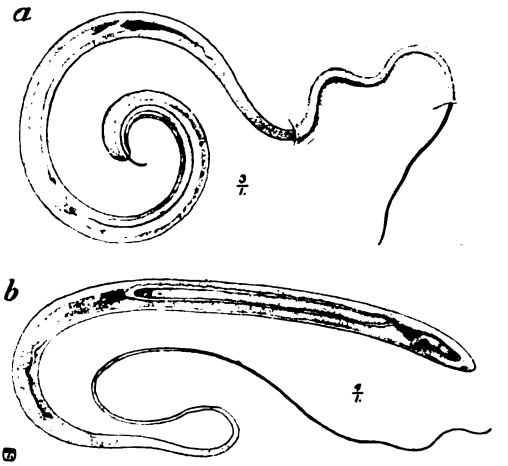


Fig. 322.—Trichuris trichiura. Magnified.

a, Male partly embedded in the mucous membrane of the intestine; *b*, female.

that the practitioner should be familiar with the appearance of its eggs in the stool (Fig. 179, *c*, p. 654), so that he may distinguish them from those of Ascaris, of Ankylostoma, and of other parasites, the presence of *T. trichiura* is of no practical moment. So far as known it gives rise to no serious pathological lesion; a fortunate circumstance, seeing that hitherto it has been found impossible, with any degree of certainty, to dislodge it by anthelmintics.

TRICHINELLA SPIRALIS (Owen, 1835)

Synonyms.—*Trichina spiralis*; *Pseudalius trichina*.

Geographical distribution.—This is worldwide. In Europe, Trichina was formerly common in Germany until the most stringent prophylactic measures were taken; in America it is still very common—in Boston, for instance, it is estimated that in the municipal slaughter-houses 5 per cent. of the pigs are infested. In Asia it has been found in China and India; and epidemics have been reported in Syria from eating the flesh of naturally-infested wild boars. In Africa it is found in Algeria and in the East African Protectorates.

Digitized by Google

It has been reported occasionally from Australia. Pigs become infested most frequently by eating garbage from the abattoirs.

The parasite (Fig. 323).—This is a white worm just visible to the naked eye. The male is 1·6 mm. in length by 40 μ in breadth; the cloaca, situated posteriorly between two caudal appendages, is provided with two pairs of papillæ. The female is viviparous, 3–4 mm. in length by 60 μ in breadth; the vulva is situated in the anterior fifth, the posterior half of the body being occupied by the ovary, the anterior by a much-coiled uterine tube. The anus is terminal.

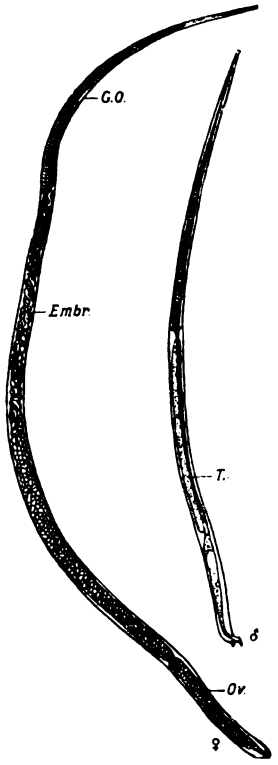


Fig. 323.—Trichinella spiralis. × 45 diam. (*After Brumpt.*)

(*G.O.*, Genital opening; *Embr.*, embryos; *Ov.*, ovary; *T.*, testis.

Life-history and pathogenesis.—The adult trichinæ inhabit the small intestine. The female being viviparous, the young which she emits emigrate into the muscles, where they encyst. In a natural state the pig, wild boar, and rat act as hosts in addition to man, but the majority of animals, even lizards, are capable of being infested under artificial conditions. Birds, however, are refractory.

Infestation of a fresh host is brought about by ingestion of raw flesh of a trichinosed animal—that is, one in whose muscles the larval trichinæ are encysted. Man becomes diseased in this manner by eating uncooked pork. The development of the adult from larvæ would appear to take place with astounding rapidity, and in as short a period as forty-eight hours after ingestion it is said that mature male and female worms can be found in the intestine. After another twenty-four hours embryos have already appeared in the uterus of the fertilized female.

The ova, measuring 20 μ, are found in the upper portion of the uterus, but soon the contained embryo breaks loose and lives freely in the uterine cavity. Some days after the invasion of the intestinal wall of their host by the females, travelling, it may be, as far as the mesenteric glands, they void the living embryos, which themselves measure now 100 μ in length by 6 μ in breadth. Travelling independently via the lymphatics and to some extent also via the venous channel, and guided by a mysterious instinct, these embryos pierce the coats of the containing vessels and encyst in striated muscular tissues, especially that of the diaphragm, the intercostal and laryngeal muscles, and those of the neck and eye as well, especially at the tendinous insertions. In these situations they may remain alive for a period of five years, if not more, but, generally speaking, they become calcified after a sojourn of a few months or years.

In order to render trichinosed meat safe for consumption it is necessary

Digitized by Google

to boil it for a period of an hour for every kilo weight of flesh. The process of curing raw ham (essentially the most common source of trichinosis) by saltpetre would appear to kill only those larvæ which are situated in the most superficial tissues, whil · those in the deeper layers escape. Curing hams by smoke, as practised in Westphalia, appears to exert no lethal action whatsoever upon the trichinæ.

Both the mature parasites and the larvæ produce the most profound pathological effects. The numerous adults cause an intense catarrhal inflammation of the intestinal canal, and by the hæmorrhages they induce may lead to death. The objective symptoms of this stage may resemble those of cholera or possibly those of dysentery, with passage of blood-stained stools, associated with hyperpyrexia (temperature 104°–106° F.). During the migration of the larvæ through the tissues typhoidal symptoms predominate, with remittent temperature and slow muttering delirium, merging into rheumatic muscular pains, difficulty in mastication, deglutition, and respiration. Three weeks after infestation, while the embryos are encysting in the muscles, a profound cachexia, probably due to absorption of the toxins from the larval trichinæ, supervenes. An œdema of the face, abdomen, and legs is often noted. Together with this there are mental apathy, intense pruritus, and sometimes skin eruptions. Death may take place in the sixth or seventh week from exhaustion or from pulmonary complications. In the cases which survive, the fever gradually resolves, but muscular pains of varied intensity persist.

As regards *diagnosis*, the early intestinal symptoms must not be confused with ptomaine poisoning, cholera, or dysentery. The debility, delirium, and remittent pyrexia may suggest typhoid ; the œdema may be mistaken for that of nephritis, though, of course, the urine is free from albumen. From these conditions trichinosis may be differentiated by the high eosinophilia of the blood, by the absence of the Widal reaction, and by the discovery of the adult worms and, in the later stages of the disease, even of the embryos in the fæces. In the more chronic rheumatoid stages the characteristic encysted larvæ can be recognized under the microscope in a small portion of muscular tissue removed for the purpose.

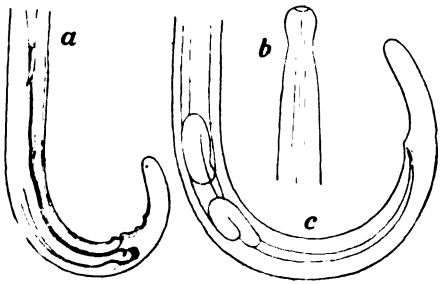


Fig. 324.—Parental forms of F. bancrofti. Magnified.
a, Tail of male ; *b*, head and neck ; *c*, tail of female.

FILARIA BANCROFTI, Cobbold, 1876

Synonyms.—*F. wücheri* (*F. sanguinis hominis*, *F. nocturna*, Manson).

Geographical distribution.—*F. bancrofti* has a wide tropical and subtropical distribution. It has been found as far north as Spain in Europe,

Digitized by Google

and as Charleston in the United States; and as far south as Brisbane in Australia.

The parasite (Fig. 324).—A long thread-like white worm found in the lymphatic glands and vessels. One or more of both sexes are generally found coiled together, and are only separable with difficulty. The *male* is 40 mm. in length by 0·1 mm. in breadth. It is generally coiled, with markedly cork-screw-like tail. The cloaca is subterminal and contains two unequal spicules (0·2–0·6 mm.); there are minute caudal papillæ arranged in two rows of 15

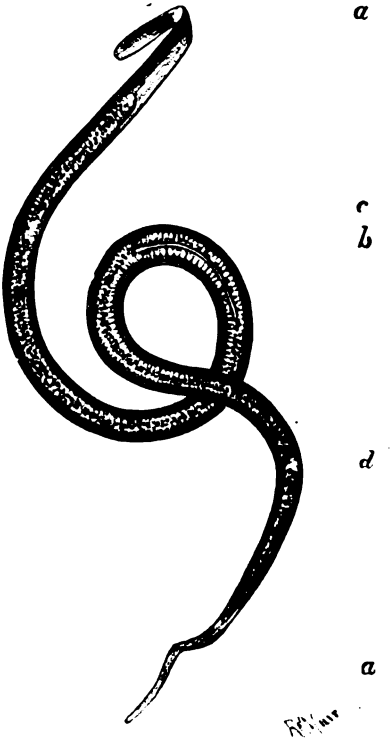


Fig. 325.—Anatomy of mf. bancrofti.

a, *a*, Sheath; *b*, central viscus; *c*, V spot; *d*, tail spot.

round the anus. The body cavity is filled with a long coiled single testis. The *female* is viviparous and considerably longer than the male; 65–100 mm. in length by 0·20–0·28 mm. in thickness. The posterior extremity is incurved, and the genital opening situated 0·6–1·3 mm. from the anterior end. Two ovaries and two much-coiled uterine tubes replete with ova and embryos in various stages of development are present. In both sexes the mouth is provided with a double row of extremely minute papillæ. The anterior extremity is tapering and club-shaped; the tail narrow, but abruptly rounded at its tip.

Digitized by Google

The ova, when extruded into the uterus, contain well-formed embryos enclosed in a membrane which subsequently becomes the sheath of the living microfilaria. These embryos emitted by the viviparous female find their

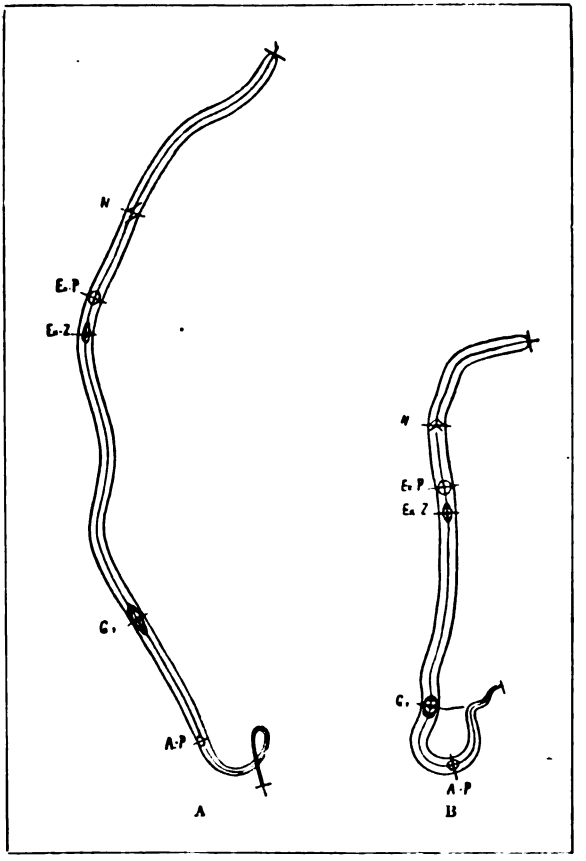


Fig. 326.—A, Scheme for the measurement of certain fixed points of structure in microfilariæ, of value in the diagnosis of species. B shows that even in a shrunken specimen the measurements retain their same proportionate value. (*After Fülleborn.*)

Measurements: 1, From the ant. extremity to the nerve ring (N.); 2, to the middle of the excretory pore (Ex. P.); 3, to the nucleolus of the excretory cell (Ex. Z.); 4, to the nucleolus of the genital cell (G_1); 5, to the middle of the anal pore (A.P.); 6, to the terminal tail nucleus.

way via the lymphatics into the bloodstream and are taken up by various species of mosquito of the genera *Culex*, *Stegomyia*, and *Anopheles*, in whose thoracic muscles they develop further.

For additional details of the pathogenesis and life-history *see* pp. 581–617.

Digitized by Google

Filaria ozzardi, Manson, 1897

Synonyms.—*F. demarquayi*; *F. juncea*, Railliet.

History and geographical distribution.—Manson first discovered the embryos of this species in aboriginal Carib Indians sent by Dr. Ozzard of British Guiana. In shape and size these embryos closely resembled *microfilaria perstans*—that is to say, they were sheathless but had sharp tails, in contradistinction to the blunted extremity of that species. They observed no periodicity and were present in the bloodstream both by day and by night. It was at first thought that similar embryos from natives of St. Vincent represented a different species, distinguished by Manson as *F. demarquayi*, but it is now generally recognized that only one species exists. As far as is known, *F. ozzardi* is confined to the West Indies and South America.

The parasite.—The parental forms of this microfilaria were first found by Daniels at the autopsy of two Demerara Indians; later, Galgey found five adult females in the omental tissues of a native of St. Lucia. In Daniels' cases they were situated in the mesentery and the visceral fat. The male measures about 32 mm. in length; the tail is much coiled and carries at least one spicule and a pair of large fleshy papillæ (Fig. 327). The female is about 65–81 mm. long and 0·210–25 mm. broad. In both sexes the head is somewhat club-shaped and bears no papillæ. The embryos (Plate XXIII., Fig. 4) are very minute, measuring 173–240 μ by 4–5 μ in diameter. As far as is known, this filaria has no pathogenic action.

Fig. 327. Caudal extremity of Filaria ozzardi, ♂, showing papillæ. (*After Leiper.*)

Filaria conjunctivæ, Addario, 1885

Synonyms.—*F. inermis*; *F. papillosa*; *F. apapillocephala*; *F. oculi humani*, v. Nordmann.

The normal hosts of this species are horses and asses, especially in South-Eastern Europe and India. There are six recorded instances of infestation in man.

The parasite.—The worms are filiform and reddish in colour, with the cuticle striated in a transverse manner. The *male* is 6–8 cm. long by 0·5 mm. in breadth, with a spirally-coiled tail provided with one delicate spicule (0·25 mm.). The *female* is viviparous, twice the length of the male, and terminates in a blunt prominence. The unsheathed embryos or microfilariæ are found in the bloodstream (350 μ by 5·5 μ).

The development is thought to take place in *Chrysops excutiens*. Recently Forbes has described the successful removal of this worm from a cystic swelling in the upper forearm, and from a fibrotic tumour of a similar nature on the nose near the inner canthus of the eye, from a Serbian in Salonica during the War.

Dirofilaria magalhaesi, R. Blanch., 1895

This filaria is of academic interest only. Magalhaes described two sexually mature filariæ in the left ventricle of a child in Rio de Janeiro. The parasites were thread-like, cylindrical, and white in colour. The oral end was club-shaped and the body tapered towards the tail. The female measured 155 mm. in length by 0·7 mm. in diameter. The male was 83 mm. in length by 0·4 mm., and its tail was provided with four pairs of preanal and four pairs of postanal papillæ and two spicules.

Digitized by Google

LOA LOA (Guyot, 1778)

Synonyms.—*F. loa ; Dracunculus oculi ; F. oculi ; F. subconjunctivalis ; F. diurna ; F. bourgi.*

Geographical distribution.—*L. loa* is widely distributed throughout tropical West Africa. It is a parasite of man, as far as is known, but, according to Plehn, the natives of the Cameroons assert that it occurs in goats and sheep.

The parasite.—The adult male worm measures 30–34 mm. in length, and presents a maximum breadth of 0·350–0·430 mm. in the anterior part of the body. (Fig. 328.) The posterior part tapers gradually towards the tail. The measurements of the adult female have not been satisfactorily determined ; the specimens so far examined, extracted from under the skin

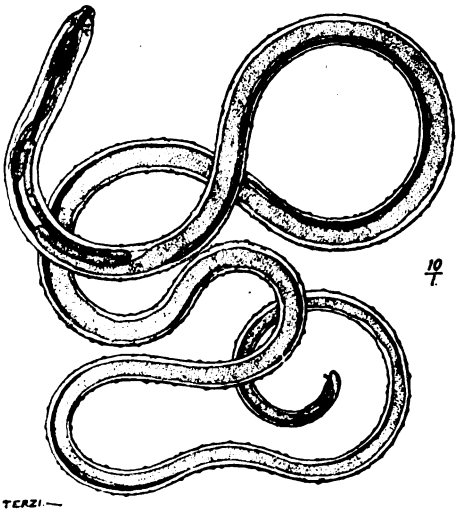


Fig. 328.—L. loa, male. (*Partly after Looss.*)

or from about the eyes of patients, varied greatly in length*—20 mm. (Blanchard) ; 27 mm. (Leuckart) ; 32·3 mm. (Manson) ; 50 mm. (Annett, Dutton and Elliot) ; 52 mm. (Looss) ; 55 mm. (Ozzard) ; 60 mm. (Brumpt) ; 70 mm. (Maurel). (Fig. 329.) The breadth is about 0·5 mm.

L. loa is especially characterized among the nematodes of man by the presence of numerous rounded, smooth, translucent protuberances of the cuticle, 12–16 μ in diameter and rising 9–11 μ above the general surface. These chitinous bosses vary greatly in number and arrangement on different specimens and are, as a rule, more numerous on the female. Their distribution is very irregular. In the male they are wanting at the extremities, beginning about 1·5–2·5 mm. from the mouth and tail-tip respectively. In

* If the record of Guyon (1864) that his specimen was 15 cm. long does not rest on an error in transcribing or printing, it shows that the fully grown female is really much larger than we know at present from the extracted subcutaneous specimens.

Digitized by Google

the female they usually extend to the posterior extremity and may also be found on the cephalic end.

The body is filiform, cylindrical, whitish, semitransparent. Anteriorly it tapers somewhat abruptly to the mouth, which is terminal, small, simple, unarmed, and apparently destitute of papillæ. There is no distinctly marked neck, but there is a sort of shoulder about 0·15 mm. from the mouth, and at about this level are two small papillæ, one corresponding to the dorsal, the other to the ventral median line.

The posterior extremity of the female is straight, attenuated, and broadly rounded off (Fig. 330). That of the male is slightly curved ventrally and provided with two lateral expansions of the cuticle (0·7 mm. long by 0·029 mm. broad), situated nearer the ventral than the dorsal surface. In the middle of the ventral surface, between the lateral alæ, and about 0·080 mm. from

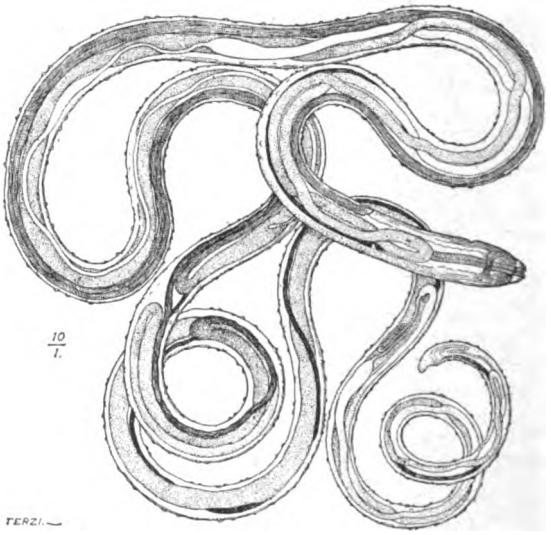


Fig. 329. –L. loa, female. (*Partly after Looss.*)

the tail-tip, is the opening of the ano-genital orifice, from which two unequal spicules may be seen protruding. The opening is surrounded by thick labia. On either side, and somewhat asymmetrically placed, are four large globular and pedunculated papillæ closely approximated and decreasing in size antero-posteriorly. Farther back, and nearer to the middle line, is a fifth symmetrical pair of very small, conical, postanal papillæ with broad base and acuminated point. (Fig. 331.) Leiper has reported the existence of three additional minute and paired papillæ.

The alimentary tube begins at the oral cavity, which is funnel-shaped and surrounded by a strong muscular mass. It consists of a slender œsophagus without bulb, of an intestine attaining a width of about 65 μ towards the middle of the body, and of a short, attenuated rectum.

The male reproductive organ is first encountered about 3 mm. from the cephalic extremity, where it ends in a pointed blind sac. Anteriorly it is

Digitized by Google

very sinuous and winds round the alimentary canal; posteriorly it straightens, attains a diameter of 85–105 μ, and terminates by a vesicula seminalis filled with more or less spherical spermatozoa 6–8 μ in diameter.

In the female the vulva forms a small eminence about 2·5 mm. from the anterior extremity. The vagina, 9 mm. long and 95 μ wide, branches off into two long tubes extending almost throughout the entire length of the body. These tubes, the narrow ends of which are the ovaria, contain eggs in all stages of development, as well as free larvæ 0·253–0·262 mm. in length by 0·0047–0·005 mm. in breadth.

The embryo, *mf. diurna*, is very similar in size (298 μ by 7·5 μ) and structure to *mf. bancrofti*. The development of the embryo outside the human body takes place in the salivary glands of certain species of Chrysops—*C. dimidiata* and *C. silacea*—and is similar to that of *F. bancrofti* in the mosquito.

For further details of life-history and pathogenesis *see* pp. 631–7.

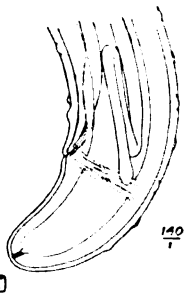


Fig. 330.—Posterior extremity of L. loa, female. (*After Looss.*)

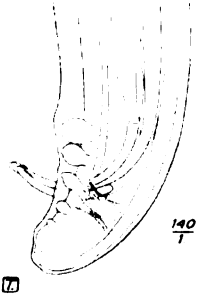


Fig. 331.—Posterior extremity of L. loa, male. (*After Looss.*)

THELAZIA CALLIPŒDA, Railliet and Henry, 1910

Synonym.—*Filaria palpebralis.*

This worm is usually found as an ocular parasite of the dog in Asia. In 1917 Stuckley in China removed four, measuring 8–13 mm., from the fornices of the left eye of his native servant; the next day he removed a similar one from the opposite side. At the same time a similar worm was found in the eye of a pet dog. A second instance was reported by Trimble, also from China, in the same year. The *male* worm is given in the veterinary text-books as 6 mm. in length; there are four preanal and one small postanal papillæ. The *female* measures 10–12 mm. in length.

ACANTHOCHEILONEMA PERSTANS, Railliet, Henry and Langeron, 1912

Synonym.—*Filaria perstans*, Manson, 1891.

The adult worm was discovered by Daniels in Demerara Indians, and subsequently identified by Manson. The embryo or microfilaria was first discovered in the blood by Manson in 1891.

Geographical distribution.—This parasite is very common in the blood of the natives of large districts in tropical Africa. Manson found it in natives from Old Calabar and from the basin of the Congo—both in the coast negroes

Digitized by Google

and in those from the interior. Annett, Dutton and Elliot reported its presence in many places in Nigeria, in the Gold and Ivory Coasts, in the Kroo Coast, and in Sierra Leone. In Northern Rhodesia it is very common; Manson found it in 30 per cent. of a number of the natives examined. On the Congo in parts it occurs in half the population. Cook, Hodges, and Low found it to be extremely common in Uganda, in some districts in 90 per cent. of the population. Sometimes it occurs along with *mf. loa*, *mf. bancrofti*, and in British Guiana with *mf. ozzardi*, in the same individual. Manson never found it in West Indian negroes, nor, in fact, in natives of any country except those of tropical Africa and in the aborigines of Demerara. He frequently found it, however, in Europeans who had resided on the Congo.

The parasite.—*A. perstans* is, like *F. bancrofti*, a long, cylindrical, filiform nematode. The body is smooth, without markings; the mouth simple and unarmed. The tail in both sexes is peculiar and characteristic; it is incurvated, and the chitinous covering at the extreme tip is split up as it were into two minute triangular appendages, giving it a mitred appearance (Fig. 332). The *male* is smaller than the female; it measures 45 mm. in length by 0·06 mm. in breadth. The diameter of the head is 0·04 mm. Close to the opening of the cloaca there are four pairs of preanal and one pair of postanal papillæ, and, according to Leiper, another small pair is situated midway between these groups. Two unequal spicules may sometimes be seen protruding from the cloaca. The adult *female* measures 70 to 80 mm. in length by 0·12 mm. in breadth. The head is club-shaped and measures 0·07 mm. in diameter. The genital pore opens at 0·6 mm. from the head. The anus opens at the apex of a papilla situated in the concavity of the curve formed by the tail. The diameter of the tail just before termination is 0·02 mm.

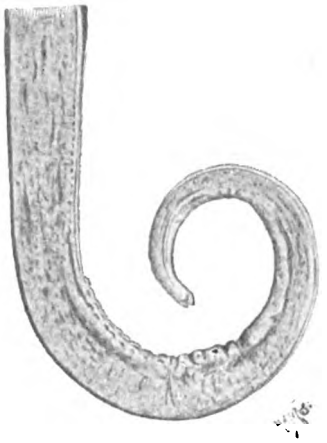


Fig. 332.—Tail of adult A. perstans.

The embryo.—*Mf. perstans* (Plate XXIII., Fig. 2) observes no periodicity, being present in the blood both by day and by night. In this respect it resembles *mf. ozzardi* (*mf. demarquayi*); and, like this, in size, shape, and anatomical detail it differs very materially from *mf. bancrofti* and *mf. loa*. The number of microfilariæ in the peripheral circulation may vary considerably, but there is no marked difference between day and night. Their special seat of selection is not the peripheral blood, but that of the heart, lungs, aorta and other large vessels. They have not been found in the spleen, and only rarely in the liver and pancreas. The embryo in the blood measures on an average 0·2 mm. in length by 0·0045 mm. in breadth; but, as it possesses in a remarkable degree the power to elongate and to shorten itself, these measurements do not always apply. It is manifestly much smaller than *mf. bancrofti* and *mf. loa*, and is further distinguished from these microfilariæ by the entire absence of a sheath and by the characters of its caudal end, which is invariably truncated and abruptly rounded off. The taper which terminates

Digitized by Google

in the tail extends through quite two-thirds of the entire length of the animal. Further, if the head be carefully observed with a high power, a fang can generally be easily seen—much more easily than the corresponding structure in *mf. bancrofti*—in constant play, shot out and retracted. The V spot is about 0·03 mm. from the cephalic extremity. There is no marked tail spot. No hooked cephalic prepuce can be made out. According to Fülleborn, no red staining "granular mass" can be demonstrated as in the case of *mf. bancrofti* and *mf. loa*. Its movements also differ from those of *mf. bancrofti*, for it not only wriggles about, just as that parasite does, but indulges in long excursions through the blood, moving freely all over the slide—locomoting, in fact, very much in the same way as *mf. bancrofti* does in the mosquito's stomach after it has cast its sheath.

So far the adult forms have been found only in the connective tissues at the root of the mesentery, behind the abdominal aorta, and beneath the pericardium.

Life-history and pathogenesis.—Very little is known of the life-history of *A. perstans*. Although it has a wide geographical range, this filaria appears to be limited in its topography to areas covered by dense forest growth and abounding in swamps. In Kavirondo, where the forest disappears and the land is covered with scrub and short grass, it is not found; likewise it is not found on the grassy plains of the highlands of British East Africa. Towns and cultivated areas are free from it. This peculiar limitation of its distribution would indicate an intermediary restricted to similar stations—certain Tabanidæ, for instance, or certain species of sylvan mosquitoes. In order to find the intermediary host of *A. perstans*, Low made numerous experiments with many different species of mosquitoes (*Culex fatigans, C. atratus, C. viridus, C. luteolateralis, C. quasigelidus; Anopheles argyrotarsis, A. costalis, A. funestus; Stethomyia nimbus; Janthinosoma musica; Mansonia africana; Uranotænia cœruleocephala; Tæniorhynchus fuscopennatus*) and other blood-sucking insects (*Pulex irritans, Sarcopsylla penetrans, Pediculus capitis*, and *P. vestimentorum*). These insects were either caught in the huts of infected persons or were reared from the larvæ and then fed on infected persons. After a certain time they were dissected, but, with one exception, the results were negative. In one isolated instance two developmental forms were seen between the thoracic muscles of a *Tæniorhynchus fuscopennatus* reared from the larva and fed on infected persons. Fülleborn has found similar developmental forms once in *An. maculipennis*. Christy suggests that the true intermediary host of *A. perstans* is *Ornithodoros moubata*, a tick of the sub-family *Argasinæ*. He gives no evidence in support of this view, which is contradicted by the facts of geographical and topographical distribution.

So far as known, *A. perstans* has no great pathological importance: the presence of the adult parasites in the mesentery appears to cause little harm to the host.

Onchocerca volvulus, Railliet and Henry, 1910

Synonym.—*Filaria volvulus*, Leuch., 1893.

O. volvulus is a parasite of the skin and subcutaneous tissues in natives of the West Coast of Africa and Guatemala, in whom it forms peculiar tumours (*see* p. 638).

The parasite.—The adult *male* is 20–32 mm. in length by 0·2 mm.

Digitized by Google

in breadth. The body is white, filiform, tapering at both ends. The head is rounded and has a diameter of 0·04 mm., and the cuticle is striated. The alimentary canal is straight and ends in a subterminal anus. The tail terminates in a single spiral and is bulbous at the tip. There are two pairs of preanal papillæ, two pairs of postanal, and an intermediate single large papilla. Two unequal spicules may be seen protruding from the cloaca (Fig. 333). The adult *female* measures 60–70 mm. in length by 0·36 mm. in breadth; more recent measurements are much less, 35–40 mm. in length (Schäfer). The head is rounded and truncated; it measures 0·04 mm. in diameter. The tail is curved. The striations of the cuticle are not so distinct as in the male. The egg possesses a peculiar striated shell.

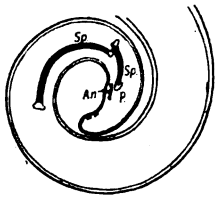


Fig. 333.—Caudal extremity of Onchocerca volvulus, ♂. (*After Brumpt.*)

Sp., spicules; *An.*, anus; *p.*, papillæ.

The embryo measures about 300 μ in length; it has no "sheath." The body tapers from about the last fifth of its length and terminates in a sharply pointed tail. At about the anterior fifth of the body there is a gap in the central column of cells (V spot).

At least four males and two females are present in every tumour.

TABLE OF LEADING DIMENSIONS OF FILARIÆ

	Filaria bancrofti	Acanthocheilonema perstans	Filaria ozzardi
	Mm.	Mm.	Mm.
Length	65 to 100	70 to 80	81
Greatest thickness	0·20 to 0·28	0·120	0·210
Diameter of head	0·055	0·070	0·050
Diameter of neck	0·040	0·054	0·039
Distance from head of vaginal outlet...	0·6 to 1·3	0·600	0·710
Distance from tail of anal papilla ...	0·225	0·145	0·230
Termination of tail	Blunt, circular, not bulbous.	Slightly bulbous; covered by thickened cuticle prolonged into two triangular appendages.	Bulbous cuticle not thickened.

Dracunculus medinensis, Velsch, 1674

Synonym.—*Filaria medinensis; Guinea-worm.*

Geographical distribution.—*D. medinensis* is a common parasite of man and animals in India and Africa.

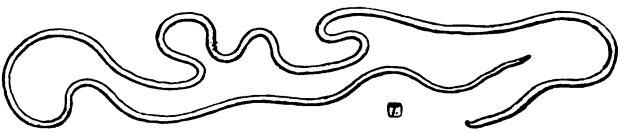


Fig. 334.—Dracunculus medinensis. One-fifth nat. size.

The parasite (Figs. 334, 335).—The female is reputed to attain in some instances enormous dimensions; it is probable, however, that worms of 5 or 6 ft. in length owe their size to errors of observation—two worms, or

Digitized by Google

their fragments, having been regarded as one. According to Ewart, in forty carefully measured specimens the smallest was about 32·5 cm., the largest 1 m. 20 cm. in length; 90 cm. is probably an average length. The diameter of the worm is about 1·5–1·7 mm. The body is cylindrical, milky-white, smooth, and without markings. The tip of the tail comes to a point and is abruptly bent, thus forming a sort of blunted hook, perhaps functioning as a "holdfast." The head end is rounded off, terminating in what is known as the cephalic shield. The mouth is triangular, very small, and surrounded by six papillæ—two large and four small. The alimentary canal is relatively small, being compressed and thrust to one side by the uterus; in the mature worm it is probably cæcal, for it has not been traced to an anus. Nearly the whole of the worm is occupied by the uterus, which is packed from end to end with coiled-up embryos. (Figs. 336, 337.) The vagina also may be lacking. According to Looss, the uterine tubes (he states, contrary to Leuckart, that there are two) open into the posterior part of the œsophagus by a common duct, the œsophagus prolapsing through the mouth at the time of parturition and being subsequently withdrawn. Leiper, however, has shown that the worm discharges its young by a prolapse of the uterus, as described by Manson, and that the extrusion does not occur through the mouth, as suggested by Looss and Manson, but by a rupture just outside the circumoral ring of papillæ, possibly the vagina.

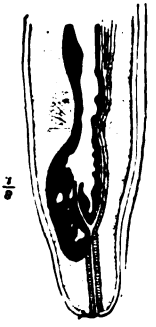


Fig. 335.—Anterior extremity of Dracunculus medinensis. (*After Leuckart.*)

Nothing definite is known of the male worm. According to Polak, the Persians have long known the male to be a smaller worm, 7–10 cm. long. They also stated that at times as many as twenty of these small worms might be found coiled round a female specimen. Charles described a shorter (4 cm.) worm, regarding it as the male, which he found twice, attached to the larger female worm within the subperitoneal connective tissue. Charles's description does not exclude the possibility that what he describes as the male worm *in coitu* was really a prolapse of the uterus through the ruptured integument. Daniels, at the post-mortem of a monkey experimentally infected by Leiper six months previously, found three immature females (30 cm. long) and two remarkably small males (22 mm.), which were obtained, one from the psoas muscle and the other from the connective tissue behind the œsophagus.

Fig. 336.—Transverse section of D. medinensis. (*After Leuckart.*)

The *embryo* measures 0·65 to 0·75 mm. long by 0·017 mm. broad. (Fig 338.) According to Looss they are flattened, not cylindrical. They are provided

Digitized by Google

with a long and slender tail, an abruptly rounded head, an easily distinguishable alimentary canal, a rudimentary anus, and a bulbous œsophagus. The cuticle is transversely striated. Towards the root of the tail are two peculiar glandular organs.

Development in intermediary host.—The embryos, when voided into water, are extremely active and may remain alive as long as three weeks. They then enter the body of several species of Cyclops (*C. quadricornis, C. strenuus, C. viridis,* and *C. bicuspidatus*), and, after casting their skins two or three times, lose their long tails, the posterior extremity assuming a trilobed appearance as in *F. bancrofti* and *F. recondita* in the mosquito and the dog-flea respectively. According to the temperature, after four to six weeks they become fully-grown larvæ, 1 mm. in length, and lie in the thorax of the cyclops. In this condition they are ingested by man.

For further details of life-history and pathogenesis *see* pp. 639–46.

Fig. 337.—Uterus of guinea-worm, showing contained embryos. × 50. (*Microphoto: Dr. J. Bell.*)

GNATHOSTOMUM SPINIGERUM (Owen, 1838)

Synonyms.—*Cheiracanthus siamensis; Strongylus siamense* (Levinsen, 1839).

History.—*Gnathostomum spinigerum* was discovered by Deuntzer in Bangkok (Siam), and described by Levinsen, who proposed to call it *Cheiracanthus siamensis.*

Geographical distribution.—So far it has been seen in Siam and Malaya only. It was met with in three patients, one of whom had five or six of these worms. Recently, Samy has recorded a specimen from a thenar abscess in a Chinese coolie in Malaya.

The parasite.—Only one female specimen was preserved and forwarded to Levinsen (Fig. 339). It measured 9 mm. in length by 1 mm. in breadth. The cephalic extremity, slightly narrower than the rest of the body, had the appearance of a rostellum surmounted by two lips and was surrounded by

Digitized by Google

eight rows of hooklets. The posterior extremity terminated in a three-lobed prominence, at the base of which the anus opened. The anterior third of the body was beset with tridentate spines, followed by scattered simple spines, which gradually became smaller and then disappeared entirely. The vulva opened a little behind the middle of the body. Subsequently, Leiper described the male—it measured 10·5 mm. by 0·6 mm., had two large fleshy lips, two unequal spicules, two preanal and two postanal papillæ. Leiper considers its normal host in Siam to be the cat.

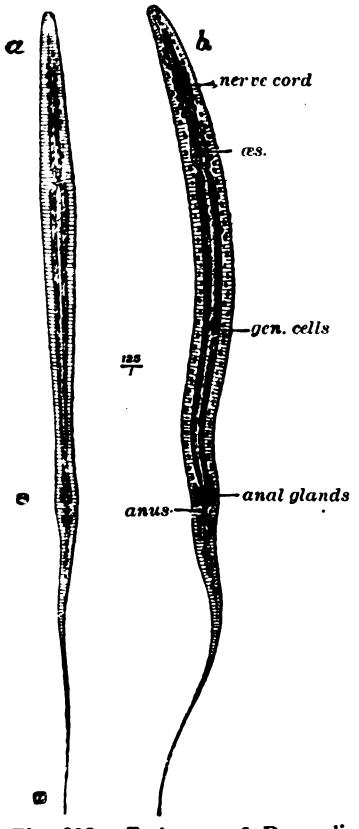


Fig. 338.—Embryos of D. mediensis. × 150.

a, Side view; *b* (*after Looss*), front view.

Life-history and pathogenesis.—We know nothing of the life-history of *Gnathostomum spinigerum*. Other species of the genus live in the stomach of various vertebrates. Before attaining maturity they are found in cysts beneath the mucosa. *G. spinigerum* is found in various kinds of wild cats (*Felis catus, F. concolor, F. tigris*). Lewis found it in the pariah dogs of Calcutta. *G. hispidum* lives in the stomach of hogs. Fedschenko found it in a Turkestan wild hog and in a Hungarian domestic hog. Csokor found it in hogs slaughtered at Vienna, Strose in Hungarian hogs, and Collin in cattle in Germany. In Vienna, butchers have long known this parasite under the name of "three-coloured worm." The parasite described by Levinsen came from a young Siamese woman, who presented a livid and painful tumefaction of the breast with slight fever. Rounded nodules the size of beans appeared at the seat of inflammation, beneath the skin. From one end of these nodules the gnathostomum protruded.

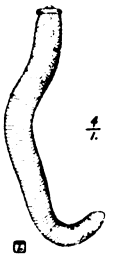


Fig. 339.—Gnathostomum spinigerum. (*After Levinsen.*)

STRONGYLOIDES STERCORALIS (Bavay, 1876)

Synonyms.—*Anguillula stercoralis; A. intestinalis; Leptodera stercoralis; L. intestinalis; Rhabdonema intestinale.*

It sometimes happens that, while searching the fæces for the ova of the ankylostoma, the observer is astonished by seeing a small, snake-like animal (Fig. 340) suddenly rush across the field of the microscope. On careful examination this animal is found to be about 0·2 mm. or 0·3 mm.

Digitized by Google

in length by 0·013 mm. in breadth; to have a sharply pointed tail and a rounded head; to be transparent; and to exhibit a short œsophagus which terminates in a double œsophageal bulb, the posterior end of which is provided with three tooth-like segments. This is the larval form of *Strongyloides stercoralis*.

The parasite.—*S. stercoralis* was discovered by Normand in 1876. For a time it was supposed to be a cause of a form of chronic diarrhœa very prevalent in Cochin China. Later investigations, while clearing up the natural history of the parasite, have robbed it of any claim to pathological importance. It has been found that, though not so common, its geographical distribution is about coextensive with that of *Ankylostoma duodenale*, and that the physical conditions demanded for the non-

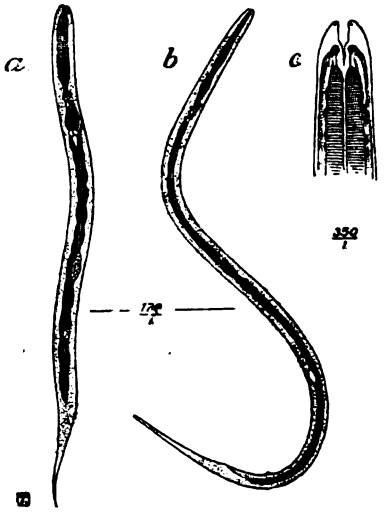


Fig. 340.—Strongyloides stercoralis. (*Partly after Looss.*)
a, Young larva from fæces; *b*, mature larva; *c*, head.

parasitic stages of these two worms are about the same. Powell found it in India in about 15 out of every 20 cases of anæmia.

The mature strongyloides (Fig. 341) is a minute, slender worm, measuring 2–3 mm. in length by 0·03 in breadth. No male parasite has been discovered. The adult female is readily recognized by her dimensions, and by the string of five or six ellipsoidal eggs (0·05 mm. by 0·034 mm.) visible about the centre of the body.

As Kanazy has shown, the parasite bores deeply into the mucous membrane of the intestine, and frequently into the epithelium of Lieberkühn's glands, both for nourishment and oviposition. The eggs develop in the intestinal wall, so that before leaving the host, unless during violent purgation, the larva has escaped and is swimming about in the fæces, as described, with great vigour, especially when these are fluid. Only in the event of violent purging do the ova appear in the stools. Such ova (Fig. 179, *d*, p. 654) are readily recognized by the way in which they are strung together,

Digitized by Google

end to end, inside a delicate tube. On leaving the host, unless they have access to some non-putrefying fluid, the larvæ soon die; it is necessary, therefore, if we would follow their further development, to mix the fæces with water. If this mixture be kept at a low temperature the young rhabditiform larva develops into a filariform larva which, on reaching its host, assumes the mature parasitic form already alluded to. If, on the contrary, the cultivating medium be kept at a higher temperature, the larvæ develop into male (0·7 mm.) and female (1·0 mm.) rhabditic forms which, in time, produce in their turn filariform larvæ similar to those obtained directly from the embryo in cold climates, and capable, on being swallowed by man, of developing into mature *Strongyloides stercoralis*.

This parasite must undoubtedly produce considerable irritation of the bowel, but its pathogenic rôle has not been definitely ascertained. It is

Fig. 341.—Strongyloides stercoralis, female. (*After Looss.*)

usually present in large numbers, and has been found occasionally coiled up in the intestinal follicles. The larvæ may pierce into the lacteals, and have been found in the blood. Van Durme, confirmed by Fülleborn, has shown that, like the larvæ of *Ankylostoma duodenale*, the filariform larvæ of Strongyloides may penetrate through the skin, and can later be found in the tracheal secretions. Hitherto the use of anthelmintics has not proved effectual in procuring their expulsion. Sonsino recommends prolonged exhibition of liquor ferri perchloridi in combination with small doses of thymol.

The prophylaxis for Strongyloides is the same as that recommended for *Ankylostoma duodenale*.

Class II.—THE GORDIACIÆ

The Gordiaciæ are nemathelminthes possessing an alimentary canal in the larval state only, and which becomes atrophied in the adult. The body is long, tapering, dark brown in colour, and adorned with cuticular expansions. The sexes are separate, and the sexual orifices are situated posteriorly.

Digitized by Google

The Gordiaciæ are free-living forms which inhabit mountain springs and wells, entangled inextricably together to the number of several dozen.

About thirteen instances of accidental infestation of man with these worms have been recorded, mostly from Italy and France. They are apparently able to live in the human stomach for three to nine months, and to produce various intestinal symptoms.

The life-history is a complicated one, and is passed within two intermediary hosts—the first an aquatic larval insect, the second a fish. Man becomes accidentally infested by drinking water containing such a parasiticized insect, and this worm, liberated by the gastric juices, completes its development in the human stomach.

Various species are recognized, of which the best-known is *G. aquaticus*.

Class III.—THE ACANTHOCEPHALA

The Acanthocephala are nemathelminthes unprovided with an alimentary canal at any period of their existence. They are elongated worms tapering at both ends, of which the anterior is provided with a protractile snout armed with spines. The cuticle is heaped up into a number of transverse ridges. The body cavity is filled with a clear liquid in which the sexual organs are suspended by a ligament. The sexes are distinct and the ova, enveloped in three shells, contain a spiny embryo. The larval stage is passed in insects, crustaceans, fish, and small mammals. The adults attach themselves to the alimentary canal, especially the small intestine, of vertebrates. Two species have been found parasitic in man.

Gigantorhynchus gigas (Goeze, 1782)

Synonyms.—*Tænia hirudinacea*, Pallas, 1781 ; *Echinorhynchus gigas*.

Geographical distribution.—*G. gigas* is a parasite in the small intestine of the domestic pig, the wild boar, and the collared peccary. It is said to occur quite frequently as a human intestinal parasite on the Volga. The worm adheres by means of its proboscis to the mucosa, which ulcerates at the point of attachment, very often through the muscular as far as the peritoneal coat; pearly nodules are thereby formed on the surface, and are said to be familiar objects to the pork-butcher.

Fig. 342.—Gigantorhynchus gigas, ♂. Half natural size. (*After Brumpt.*)

The parasite (Fig. 342).—The adult is a white worm with a transversely striated cuticle. The proboscis has five or six rows of curved hooks, and can be retracted into the neck, which is the thinnest part of the body. The male is 5–10 cm. in length, 3–5 mm. in breadth, and has a globe-shaped caudal bursa; the female is 20–35 cm. in length by 4–10 mm. in breadth; the posterior termination is blunt. The anus is terminal, the vagina subterminal.

The ova (Fig. 343) are elliptical, 80–100 μ in length, and are covered with three envelopes, of which the external layer is pitted. The embryo is doubled up inside the shell, which it completely fills, and is armed on its anterior aspect with minute hooklets.

Life-history and pathogenesis.—In Europe the larval forms inhabit the cockchafer grub, *Melolontha vulgaris;* in the United States the inter-

Digitized by Google

mediary host is another coleopteron, *Lachnosterna arcuata*. In the animals it infests *G. gigas* is capable of producing a catarrhal inflammation of the gut and, it may be, actual perforation.

GIGANTORHYNCHUS MONILIFORMIS (Bremser, 1811)

Synonym.—*Echinorhynchus moniliformis.*

Geographical distribution.—*G. moniliformis* is a common parasite of the rat in Europe, Africa, and Brazil. It has been found parasitic in man in Italy by Grassi and Calandruccio, and by Christopherson in Khartum.

The parasite.—A white worm, attenuated at both extremities; the middle portion of the body is embossed with nodosities which give it the appearance of a porocephalus. The proboscis is long, 450 μ, and is furnished with 15 rows of hooklets arranged in a transverse manner. The male is 4–5 cm. in length, and the female 7–10 cm.

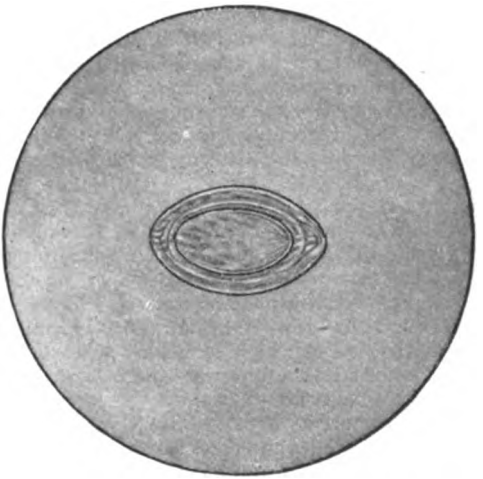


Fig. 343.—Ovum of Gigantorhynchus gigas. × 250.
(After a microphoto by Dr. J. Bell.)

The ova are elliptical in shape, 85 μ in length by 45 μ in breadth; the embryo is striated and well provided with spines.

Life-history and pathogenesis.—The intermediary host of this parasite in Europe is a coleopteron larva, *Blaps macronata*, though experiments conducted by Calandruccio showed that auto-infestation of the definitive host may occur.

PHYLUM ANNELIDA

The Annelida of medical interest comprise the leeches, which have been treated, so far as their pathological effects are concerned, in the text. Zoologically speaking, they are bilaterally symmetrical worms with a moist cuticle and a body composed of segments or *somites*, placed in mathematical order one behind the other. The body is cylindrical in shape or flattened in a dorso-ventral direction. The body cavity is well developed, and there

Digitized by Google

is a self-contained blood vascular system. The excretory system is represented by *nephridia*, two to each segment, with corresponding canals opening to the exterior. The *alimentary canal* runs direct from mouth to anus, situated respectively at the anterior and posterior extremities.

The *nervous system* is represented by a ventral ganglionic nerve chain dividing in front to enclose the intestinal canal. These worms are hermaphroditic; the genital orifices are two in number, the superior one being the male genital opening, situated on the 27th somite, the inferior being the female aperture, situated on the 29th somite. The former may contain, in certain genera, a penis, in others a spermatophore. In the neighbourhood of these two openings there is a depression in the body surface which is known as the *clitellum*, in which the egg-cocoon is formed.

The extremities of the Hirudinea are provided with two strong muscular suckers, the anterior of which surrounds the mouth. The oral aperture contains three or more saw-like teeth which pierce the skin of the host. The mark that is thus left is generally triangular in shape; the blood sucked from the wound by the muscular pharynx passes through the œsophagus into a diverticulated crop. Here the blood is stored until it is passed into a small globular stomach, where it is gradually digested. Certain salivary glands secrete a substance into the pharynx which prevents the coagulation of the blood.

Both free-living and parasitic leeches are recognized. The class Hirudinea is divided into a number of orders, the *Acanthobdella*, the *Arhynchobdella*, and the *Rynchobdella*. The leeches of medical interest—the genera *Hirudo*, *Limnatis*, and *Hæmadipsa*—mostly belong to the second group. The third order comprises the genus *Hæmenteria*, which is employed as the medicinal leech in Central America, and *Placobdella*, which is found in Central Europe and North Africa, and which by choice, when adult, attacks man, certain mammalia, and tortoises, but when immature lives on frogs.

A study of the intestinal contents of the water leeches is of interest from the point of view of comparative parasitology, for these annelids act as intermediary hosts for trematodes and cestodes of birds, as well as for trypanosomes of fishes and frogs. It has been suggested that certain species of land leeches, as, for instance, *Hæmadipsa zeylanica*, may transmit flagellates of the genus *Herpetomonas*.

The eggs are laid in a cocoon and hatch in water.

PHYLUM ARTHROPODA

The Arthropoda are bilaterally symmetrical metazoa with a body composed of a series of segments, so articulated with one another as to be more or less movable. The body is covered with a chitinous exoskeleton, sometimes impregnated with calcium salts. These segments bear paired and jointed appendages, so grouped together as to form three regions clearly separated from one another. The first of these is the head, which carries two pairs of antennæ, the eyes, which may be simple or compound, and the mouth part, surrounding the mouth. The second is known as the thorax, and bears on its ventral aspect the legs, used either for progression or for seizing the prey. On the dorsal aspect one or two pairs of wings may be present. The third segment is known as the abdomen, which may, or may not, bear jointed appendages, and contains the greater portion of the alimentary canal, with the anus opening at its termination. The head and

Digitized by Google

thorax may be fused together to form a cephalothorax. The body cavity is fully developed, and there is an open blood vascular system which lies dorsally to the alimentary canal. The nervous system is represented by a nerve cord which lies ventrally to the alimentary canal and anteriorly surrounds the œsophagus. Respiration is maintained by means of gills, air-tubes, or lung-books, or the oxygen may be absorbed entirely by the skin.

The sexes are separate, and there is often a marked sexual dimorphism.

The Arthropoda are subdivided into a large number of classes, certain members of which are of medical interest.

Class I.—The Crustacea

The Crustacea are aquatic forms. The body is mostly composed of a cephalothorax and an abdomen, both of which bear jointed appendages; those of the latter are used for swimming. The head bears two pairs of antennæ. Respiration is maintained by means of gills. Examples of tropical interest are cyclops, the intermediary host of the guinea-worm and of *Dibothriocephalus latus*, and the various crabs which act as intermediaries for *Paragonimus westermanni*. This class is so large and complex that works on general zoology must be consulted for further details.

Class II.—The Arachnida

This class comprises free-living and parasitic forms. The body is composed, as in the crustacea, of cephalothorax and abdomen, though the latter may have no definite demarcation. Antennæ are absent; the exoskeleton is soft. The cephalothorax in the adult bears four pairs of jointed legs. Respiration is carried on either through the skin or by means of air-tubes and lung-books. The sexes are separate, and eggs are laid, from which young similar to their parents are hatched out, growing into adults after several moults. Examples of medical interest are spiders, scorpions, mites, and ticks.

Class III.—The Insecta

The Insecta are a large group comprising insects in which the body is divided clearly into head, thorax, and abdomen. The head bears only one pair of antennæ, and the thorax only three pairs of jointed legs and, it may be, one or two pairs of wings. The abdomen is free. Respiration is effected by means of air-tubes. There are two compound eyes and two or more simple ones. The sexes are separate; the female may lay eggs or be viviparous. A metamorphosis of the larva may occur. The examples of medical interest are the flies, mosquitoes, fleas, lice, and bugs.

Class II.—ARACHNIDA

This class comprises orders including parasitic forms, the *Acarina* and the *Linguatulidæ*, and others of medical interest.

Order i.—THE ACARINA

The Acarina have a short abdomen which is fused with the cephalothorax to form a single structure. The larvæ have only three pairs of legs; the eyes may be absent or very small. Respiration takes place by means of air-tubes or through the skin. The order contains three families, Sarcoptidæ, Demodecidæ, and Ixodidæ.

(*a*) The *Sarcoptidæ* live on the surface or burrow into the skin. The

Digitized by Google

cuticle is transversely striated, and the adult has four pairs of rudimentary legs; eyes are absent.

(*b*) The *Demodecidæ* are minute arachnids living in the hair-follicles and sebaceous glands. The abdomen is elongated and finely striated; the legs are rudimentary.

(*c*) The *Ixodidæ*, or ticks, live as temporary parasites on mammals, birds, and reptiles. They are of relatively large size and have a firm, hard cuticle. After a meal the body becomes greatly distended. Respiration is effected by means of air-tubes. The adults are provided with four pairs and the larvæ with three pairs of legs.

(*a*) Sarcoptidæ (*including the Itch- and Scab-Mites*)

Sarcoptes scabiei (Linn., 1758)

Synonym.—*Acarus scabiei.* (Figs. 344, 345.)

This is the ordinary itch-mite of common interest, and is adequately treated in most textbooks. The female is 0·3–0·4 mm. in length, the male 0·2 mm. The latter is provided with a penis situated at the fourth pair of legs. The gravid female lives in a burrow in the skin, at the entrance of which the male keeps watch. The eggs, measuring 150 μ by 100 μ in breadth, are laid in the burrow, and give rise to larvæ which pass through four stages in a period of six weeks, as follows: Firstly, a hexapod larva, which moults several times and becomes an octopod nymph, characterized by twelve dorsal spines. The third stage is entered about the twenty-eighth day, when the nymphs moult and become sexual males and females, which pair off. During the fourth stage, that is at the sixth week, the impregnated female moults once more and develops a sexual orifice; she then burrows into the skin and deposits the eggs.

Certain host species of Sarcoptes are found on various animals which, although morphologically identical with the human itch-mite, can only maintain a temporary existence on the human skin. These mites are found parasitic on horses, sheep, oxen, goats, camels, llamas, pigs, foxes, wolves, rabbits, rats, and cats. The camel variety, *S. scabiei* var. *cameli*, caused a considerable amount of disability among the camel detachments in Egypt and Palestine during the War. The amount of cutaneous irritation they produced on the men of the Camel Corps was very great, but it was found that these parasites were only capable of living five days on the human skin and were unable to breed. To prevent the spread of an epidemic it is necessary to separate the men from the animals for that period in order that the latter may become disinfested.

Prevention and treatment of scabies.—The promiscuous use of blankets and the lack of washing facilities aid in the spread of the disease. Preparatory to treatment the patient should be well washed in a hot bath at 106° F. containing 2 oz. of washing soda. He should be instructed to immerse himself in this for twenty minutes. The body is then scrubbed well with soft soap and a scrubbing-brush, the hands with a stout tooth-brush. The burrows are thus torn open and the acari removed or exposed to the parasiticide. After drying, the patient is rubbed all over with a piece of list dipped in 3 oz. of *liquor calcis sulphuratus*, B.P.; it is important that a fresh solution should be used for each case. If the skin is very sensitive it may be necessary to dilute the solution at first. If this solution cannot be obtained, *unguentum sulphuris*, 2 oz. at a time, should be thoroughly

Digitized by Google

rubbed in for at least twenty minutes. The treatment of scabies by sulphur fumigation is useless.

The Sarcoptidæ contain other mites parasitic on beetles, birds, bats, etc., and a sub-family, the *Tarsonemidæ*, which are minute, soft-bodied, transparent mites, parasitic on plants, but which may become temporary parasites on man and give rise to an intolerable itching by excretion of some venomous substance. In this family the cheliceræ are pointed, the pedipalps are hardly visible, and the last two pairs of legs are placed far behind the anterior pair. *Pediculoides* (Figs. 215–17, p. 728), especially the species *P. ventricosus*, is parasitic on insects, and is often found in raw cotton, which has given rise to epidemics of itch among stevedores unloading cotton ships. The abdomen of the pregnant female of this species becomes swollen with eggs, like a small chigger. In it the eggs hatch and the young complete their development, to issue forth as adults.

The family *Tyroglyphidæ*, or cheese-mites, are minute, light-coloured creatures with a distinct cephalothorax; the legs are of a moderate length, often terminating in a sucker. These insects, which are found in flour, dried fruit, cheese, and copra, occasionally infest the skin of grocers who handle these substances, causing an erythema known as "grocer's itch," and, in the case of copra dealers, "copra itch." The insects are sometimes passed intact through the alimentary canal, and may appear in the stool, where they may be found on microscopic examination. (Fig. 393, p. 905.)

The family *Trombidiidæ* are large, bright-red mites, known as velvet mites, predaceous on their own kind and other insects, while some are very destructive to plants. The larvæ of this family may infest the human skin, causing very severe itching, and are known as harvest-bugs. The orange-coloured larva, *Leptus autumnalis*, 0·5 mm. in length, is produced from eggs which are deposited by the parents on the ground. (Fig. 346.) The adult, a free-living mite, *Trombidium holosericum*, is velvety red in colour, 3–4 mm. in length. The cephalothorax bears on its dorsal surface a shield composed of many hairs; at the posterior end are sessile eyes. The abdomen is transversely striated on its ventral surface; there are three pairs of legs, and a prominent stigma at the base of the first pair. The rostrum is provided with a pair of pedipalps bifurcating at their termination. Normally this mite is parasitic on moles and hares; it only lives for a few days on man. Inunction with oleum cajuputi or bandaging the irritated part with a weak solution of subacetate of lead or sulphate of copper gives relief.

Another species of medical interest is *Trombidium akamushi*, the Kedani mite, or intermediary host of the virus of Japanese river fever. (Figs. 70, 71, p. 242.) It is the hexapod larval form of a mite (*Trombicula akamushi*), and lives on the field-mouse (*Microtus*), the house-rat of Formosa (*R. rattus rufescens*), and other rodents. The adult form, or *Trombicula*, is found in the soil of infested fields; it is a tiny creature 0·9 mm. in length by 0·5 mm. in breadth, is pale grey or red in colour, with two rudimentary eyes and four pairs of legs; the anterior pair are stout, and are carried on the anterior part of the cephalothorax parallel to the pedipalps. The eyes are rudimentary. On the ventral surface are situated two pairs of suckers close to the genital orifice and the anus. The larva measures 0·4 mm. in length by 0·25 mm. in breadth, and resembles that of *T. holosericum* in general appearance, but the legs and pedipalps are stouter, and the body, including the legs, is covered with minute plumose hairs. The cephalothorax bears a pair of eyes conspicuously red in colour. The nymph has a peculiar figure-of-

Digitized by Google

eight shape, an abdominal constriction dividing the body into two parts: it measures 0·65 mm. in length, and in due season moults and becomes adult.

Harvest-bugs occur in practically every part of the world, and are especially annoying in some parts of the tropics. In Surinam there is a very virulent form known as *Acarus balatus*; in New Guinea and Celebes the *Microtrombidium wichmanni*, in South America the *Microtrombidium molestissimum*, known as "Bicho Colorado," are the best-known.

(*b*) Demodecidæ

DEMODEX FOLLICULORUM var. HOMINIS (Simon, 1842)

This parasite (Fig. 347) lives in the hair-follicles and sebaceous glands round the mouth and nose of man. Similar species are met with in most domestic animals, as in the case of *Acarus*. They are of interest to the tropical practitioner in that they may be considered possible intermediary hosts of blood

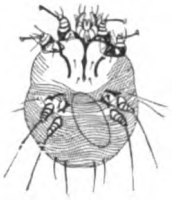


Fig. 344. — Sarcoptes scabiei: ventral aspect. × 35 diam. (*After Canestrini.*)

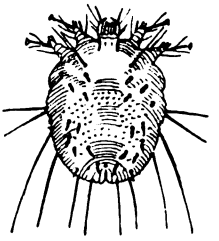


Fig. 345. — Sarcoptes scabiei: dorsal view. × 40 diam. (*After Brumpt.*)

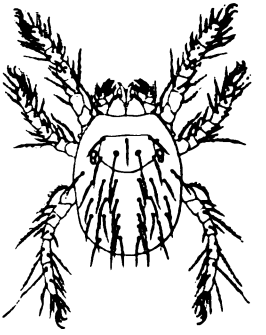


Fig. 346.—Leptus autumnalis. × 50 diam. (*After Hirst, "Journ. Economic Biol."*)

Fig. 347. Demodex folliculorum. × 10 diam. (*After Brumpt.*)

parasites. These acarines are very minute, 0·3–0·4 mm. in length. The abdomen is marked off from the cephalothorax, and is elongated and transversely striated. The anal opening is situated at the junction of the cephalothorax and abdomen. The head is provided with a prominent rostrum; there are no vestiges of eyes; the mouth is adapted for sucking and is provided with various rudimentary appendages. The cephalothorax has four pairs of very short and stumpy legs with terminal rudimentary claws. These parasites live with their heads inserted deeply into a hair-follicle. In order to demonstrate them, one should express the sebum from the mouth of the sebaceous glands or comedones and examine under a microscope in a drop of oil or xylol. If the condenser is shut down, one can distinguish the different larval stages.

Life-history.—The female lays heart-shaped ova, 60–80 μ long and 40–50 μ broad, which on hatching give rise to hexapod larvæ; after moulting several times these become sexually mature. All stages of development are passed within the follicles, but the mature parasites are believed to migrate over the skin. As regards their pathogenic rôle, they are responsible

Digitized by Google

for inflammation of the eyelids when they occur in the Meibomian glands. They have even been accused of causing epithelioma and of conveying leprosy.

(c) Ixodidæ

The ticks are cosmopolitan in their distribution, and are interesting as intermediary hosts of various protozoal diseases. With the exception

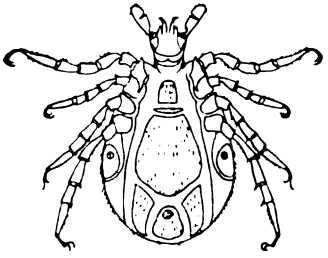


Fig. 348.—Ixodes ricinus. (*After Nuttall.*)

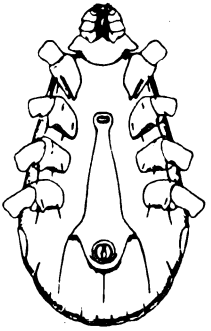


Fig. 349. — Rhipicephalus sanguineus. (*After Nuttall.*)

Fig. 350.—Boophilus decoloratus. (*After Nuttall.*)

of *Argas* and *Ornithodoros*, they rarely voluntarily attack man in the adult state. These two species are of importance as the carriers of African relapsing fever, of which further details are given on p. 186. The classification of the ticks is a very large subject and is outlined in the Table on p. 858.

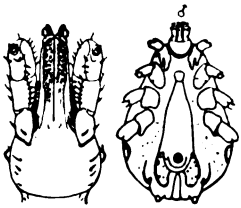


Fig. 351.—Hyalomma ægyptum. (*After Nuttall.*)

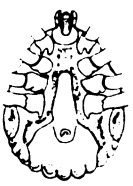


Fig. 352.—Amblyomma. (*After Nuttall.*)

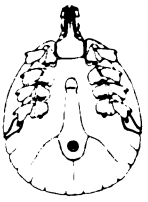


Fig. 353.—Aponomma. (*After Nuttall.*)

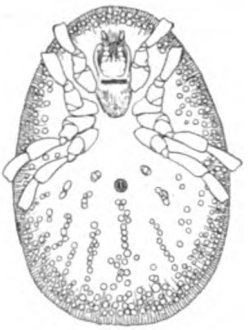


Fig. 354.—Argas. (*After Nuttall.*)

The cephalothorax and abdomen are fused to form a single structure, and the body is covered with a leathery cuticle, which in the hard ticks (*Ixodinæ*) is partly chitinous, to form a dorsal shield, or scutum. The mouth-parts are characteristic and are borne by the capitulum, which may project anteriorly or be embedded in the cephalothorax, as in Argas and Ornithodoros. From the dorsal surface of the rostrum there pass forward two

Digitized by Google

GENERIC CLASSIFICATION OF TICKS (Figs. 348–54)

Rostrum terminal. *Dorsal shield* present. *Sexual dimorphism* marked — **Family IXODIDÆ**

- ***Anal groove*** surrounding anus in front. — ***Prostriata*** — **IXODINÆ**
  - Inornate, without eyes and without festoons. Spiracles round or oval. Palps of variable form. Tarsi without spurs. *Sexual dimorphism* pronounced. In the ♂ the venter is covered by non-salient plates; one pregenital, one median, one anal, two adanal, and two epimeral plates. Parasitic on ungulata, carnivora, rodents, marsupials (kangaroo), bats, and birds. — **1. Genus IXODES.**
- ***Anal groove*** containing anus behind. — ***Metastriata***
  - (*a*) *Brevirostrata.* Rostrum short.
    - Inornate, without eyes but with festoons. Usually with short conical palps, whose second articles project laterally. Small size and slightly chitinized. *Sexual dimorphism* slight. The ♂ shows no ventral plates or shields. — **2. Genus HÆMAPHYSALIS.**
    - Usually ornate, with eyes and festoons. Short, broad, or moderate palps, and basis capituli rectangular dorsally. Spiracles sub-oval or comma-shaped. — **3. Genus DERMACENTOR.**
    - Inornate, with eyes and festoons. Short palps, with basis capituli hexagonal dorsally with prominent lateral angles. The ♂ resembles *Rhipicephalus* dorsally, *Dermacentor* ventrally. Spiracles sub-triangular or comma-shaped. — **4. Genus RHIPICENTOR**
    - Usually inornate, with eyes and festoons. Short palps, and basis capituli usually hexagonal dorsally. The ♂ possesses a pair of adanal shields and usually a pair of accessory adanal shields. Spiracles bluntly or elongate comma-shaped. — **5. Genus RHIPICEPHALUS.**
    - Inornate, with eyes, but indistinct festoons. Short palps, and capitulum intermediate between that of *Rhipicephalus* and *Boophilus*. Highly chitinized. The ♀ with very small scutum. The ♂ with a median plate prolonged into two spines projecting beyond and to either side of the anus. Anal groove obsolete. Spiracles rounded or short, oval in both sexes. — **6. Genus MARGAROPUS.**
    - Inornate, with eyes, but indistinct festoons. Very short compressed palps ridged dorsally and laterally. Basis capituli hexagonal dorsally. Slightly chitinized. Unfed adults of small size. The ♀ with small scutum. The ♂ with adanal and accessory adanal shields. Spiracles rounded or oval in both sexes. No anal groove. — **7. Genus BOOPHILUS**
  - (*b*) *Longirostrata.* Rostrum long.
    - Ornamentation absent or present, at times confined to the legs; with eyes, with or without festoons. Long palps. Basis capituli subtriangular dorsally. The ♀ approaching *Amblyomma*. The ♂ with a pair of adanal shields and with or without accessory adanal shields, and two posterior abdominal protrusions capped by chitinized points. Spiracles comma-shaped. — **8. Genus HYALOMMA.**
    - Generally ornate, with eyes and with festoons. Long palps, of which the second article is especially long. Basis capituli of variable form. The ♂ without adanal shields, but small ventral plaques are occasionally present close to the festoons. Spiracles sub-triangular or comma-shaped. — **9. Genus AMBLYOMMA.**
      - Sub-genus *Aponomma.* Devoid of eyes, or in which the eyes are poorly developed. Body frequently very broad. Occur almost exclusively on reptilia.

Rostrum concealed by overlapping cephalothorax. *Dorsal shield* absent. *Sexual dimorphism* slight. — **Family ARGASIDÆ**

- *Body* usually flat with thin edges. *Ventral grooves* absent or very shallow. *Eyes* absent . . . . . — Genus ARGAS.
- *Body* with thick edges. *Ventral grooves* present. *Eyes* sometimes present . . . . . — Genus ORNITHODOROS.

Digitized by Google

cheliceræ, one on each side of the middle line, provided terminally with hooks. On the ventral surface is situated a symmetrical hypostome, armed with files of strongly recurved teeth; this aids the cheliceræ in boring through the skin. The whole of these structures is covered on the dorsal aspect by a sheath, an expansion of the capitulum. Laterally placed to the cheliceræ are two stout, jointed pedipalps, which are thought to form an adjustable sheath for the delicate mouth-parts, and are frequently hollowed on their inner surface for this purpose. During haustellation these pedipalps are deflected. On the ventral surface of the body are four pairs of legs, each consisting of six segments terminating in a pair of claws and, in some cases, a membranous plate, or *pulvillus*, as well. A curious organ, known as Haller's organ, olfactory in function, is found in the cuticle of the tarsus or terminal joint of the first pair of legs. The genital pore, in both sexes, is situated on the ventral surface behind the capitulum. Posterior to it, in the median line, lies the anus. The spiracles, or breathing openings, lie behind the coxæ, or basal joint, of either the third or fourth pair of legs. The mouth is situated between the cheliceræ and the hypostome, and leads into a pharynx, a slender œsophagus, and a large stomach provided with cæca. The large salivary glands extend throughout the length of the body and open near the base of the hypostome; their secretion is in some cases very irritating, and may possibly cause a peculiar paralysis (*see* p. 239).

The excretory organs are represented by two long Malpighian tubules which open into the hindgut; these are supplemented by coxal glands which open on to the coxæ. Eyes, when present, are situated as minute black spots on the edge of the scutum; there may be two or even three pairs. The life-history is given on p. 186.

Order ii.—THE LINGUATULIDÆ (PENTASTOMIDÆ)

The Linguatulids are degenerate arachnids having neither eyes nor feet. The body is annulated, giving them a rough resemblance to a tapeworm. The mouth is surrounded by two pairs of primitive appendages. On the head are numerous symmetrically arranged papillæ. The opening of some large epidermal glands is situated at the base of the mouth-parts. Respiration is carried out by cutaneous absorption. Part of the life-history is passed in an intermediary host. Three genera are at present recognized—*Linguatula*, *Porocephalus*, and *Reighardia*. Examples of the former two have been found in man; the third is only met with in birds and snakes.

Linguatula serrata, Frölich, 1789

Synonyms.—*Tænia rhinaria*, Pilger, 1802; *Pentastoma tæniodes*, Rud., 1819.

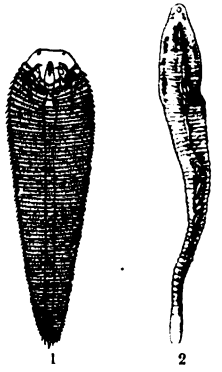
This linguatula (Fig. 355) is found in its adult state in the nasal cavity of dogs, wolves, and foxes; rarely in sheep and goats. The larvæ are met with frequently in the mesenteric glands of domestic animals as well as in rabbits and hares. They have often been found in the liver of man, in whom they appeared to cause no symptoms. In Dresden Zenker found them in 4·6 per cent. of autopsies; and they have been reported from Brazil as an intestinal parasite. The infection seems to be acquired through eating raw vegetables contaminated by the nasal secretion of dogs.

The parasite.—The body is somewhat pear-shaped and flattened, and transversely striated with about 90 rings; the mouth is roughly quadrangular in shape and surrounded by hooks. The intestine is simple. The male

Digitized by Google

is white, 18–20 mm. long, and measures 3 mm. broad anteriorly, 0·5 mm. posteriorly. The female, 8–10 cm. in length, is grey in colour, but may be brown when packed with eggs; anteriorly she measures 8–10 mm. broad, posteriorly 2 mm. The eggs are ovoid and 90 μ in length by 70 μ in breadth.

Life-history.—The eggs contain ripe embryos when they are deposited by the female, and pass out with nasal mucus to become attached to grass and other herbs; they are then ingested by the definitive host, penetrate the intestinal coats and enter the viscera, the liver, lung, mesenteric glands, kidney, etc. The larva, having grown to 5–6 mm. in length, encysts, and is ingested by various carnivora. It then migrates from the stomach, and grows into the adult form in the nasal fossæ of these animals.



1 2

Fig. 355.—Linguatula serrata. (*After Brumpt*)

1, Larval form (× 6 diam.); 2, mature form (nat. size).

POROCEPHALUS ARMILLATUS (Wyman, 1848)

Synonyms.—*Linguatula armillata; L. constricta; Pentastomum constrictum.*

History.—The larval form of this vermiform arthropod, belonging to the genus *Porocephalus*, was discovered in 1847 by Pruner in Cairo; he found it in the livers of two negroes. Subsequently it was found in man by Bilharz, Fenger, Kearney, Crawford, Marchoux, Chalmers, and others. Shipley, in his revision of the family *Linguatulidæ* (1898), points out that the adult form was discovered and named *Linguatula armillata* in 1848 by Wyman, who found it in the lungs of an African python. He also states that, in accordance with the rules of zoological nomenclature, the generic name for the cylindrical *Linguatulidæ* should be *Porocephalus*.

Geographical distribution.—*P. armillatus* seems to be confined to tropical Africa, and hitherto, as regards man, to negroes only, among whom it is far from being uncommon. Salm has found a porocephalus encysted beneath the serous coat of the small intestine of a Djambi native in Java. He gives no description, but mentions it under the name *Porocephalus moniliformis*, together with similar parasites found in the Indian civet and in the tiger.

Zoological distribution.—The adult form inhabits pythons and other snakes. It has been found in *Python sebæ*; in the royal python (*P. regius*), and in the nose-horned viper (*Bitis nasicornis*). The larval—or, more correctly, the nymphal—form has been found in the lion, in the leopard, in the mandrill, in the aard-wolf, in the giraffe, in Syke's monkey (*Cercopithecus albigularis*), in the Pousargues guenon (*Cercopithecus pousarguei*), and in the African hedgehog (*Erinaceus æthiopicus*).

The parasite (Fig. 356).—Body vermiform, yellowish, translucent, larger in females (9–12 cm. long by 5–9 mm. broad) than in males (3–4·5 cm. long by 3–5 mm. broad); cylindrical in the anterior half, slightly tapering posteriorly, and terminating in a blunt-pointed cone. It is characterized by the presence of prominent opaque rings 1–2 mm. wide, numbering 16 or 17 in the males, 18 to 22 in the females, placed somewhat obliquely and separated by interannular spaces 2·5 mm. wide, except between the first rings, which are faintly indicated by shallow linear furrows. There is no

Digitized by Google

clear distinction between cephalothorax and abdomen, and the rings nearest the cephalothorax are sometimes so indistinct that it is almost impossible to make out their actual number. The cephalothorax is depressed, slightly convex on the dorsal surface, more or less concave on the ventral surface. It is rounded anteriorly; posteriorly it is limited by the first body rings.

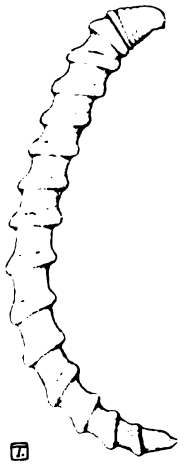


Fig. 356.—**Porocephalus armillatus.** Nat. size. (*After Sambon.*)

It varies considerably in length; its breadth is from 4 to 7 mm. The mouth, opening on its ventral surface about 1 mm. from the anterior border, is lipped by a chitinous ring. Above it are two prominent papillæ. On either side of the mouth are two protractile chitinous hooks similar in shape to feline claws. The anus is terminal at the posterior end. The genital orifice of the male is at the anterior end of the abdomen, in the middle of the ventral surface of the first body ring; that of the female opens in the middle of the ventral surface of the caudal cone at about 1 mm. from the anus. The female is oviparous; the eggs are broadly elliptical.

The nymphal form (Fig. 357) is usually found spirally coiled within a cyst, the ventral surface corresponding, as a rule, to the convexity of the curve. In shape and structure the nymph closely resembles the adult, and the number of rings is the same. Calcification of the nymphal form in the liver may take place.

Life-history.—Little until lately was known of the life-history of *P. armillatus;* it is similar to that of the European linguatulid (*Linguatula serrata*). The ova, disseminated by snakes harbouring the adult form, reach the intermediary host probably with its food or drinking-water. That this is the probable route in man is shown by the work of Broden and Rodhain, who gave porocephalus eggs to sleeping-sickness patients, and afterwards found the nymphal forms in their livers at autopsy. After entering the stomach the larvæ penetrate the mucosa, where some remain (Fülleborn); others pass on and become encysted in almost any organ or tissue, more especially liver, mesentery, or lungs. At a certain stage of development they escape from their cysts and migrate to the serous cavities, where they cause considerable inflammation. As a rule, at this stage they are swallowed by their definitive host.

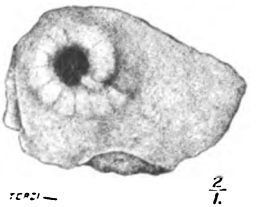


Fig. 357. — **Nymph of Porocephalus armillatus.** (*After Sambon.*)

Pathogenesis.—There is much uncertainty as to the pathogeny of this parasite. Some consider it quite harmless. There can be no doubt as to the gravity of a heavy infection at the time when the parasites are migrating in their intermediary host. In Kearney's case, reported by Aitken, twenty or thirty parasites were found encysted in the liver and one or two in the lungs. The lungs were greatly congested. In Marchoux and Clouard's case the parasites were found in the liver and in the mesentery all along the intestine, but especially about the cæcum. In Chalmers' case numerous

Digitized by Google

parasites were found moving freely in the abdominal cavity over the surface of the various organs. A large number were found within the lumen of the small intestine. Many were still encysted in the lungs.

That this worm is pathogenic to monkeys when present in large numbers was shown by Fülleborn's experiment, in which one monkey died after 60 days, the other 300 days after being fed upon the tracheal mucus of infested snakes.

It has been found accidentally in man, as in the following instance: Capt. J. Tudor Thomas, R.A.M.C., whilst operating on a case of inguinal hernia in an African soldier at Dar-es-Salaam in 1918, found a larva of porocephalus embedded in the wall of the hernial sac. This is believed to be the first occasion on which one of these larvæ has been obtained from man during life.

The diagnosis of porocephalus infestation during life is impossible.

Order iii.—THE SCORPIONIDA

This order comprises the scorpions, which are found in all parts of the tropics. Their sting, at the tip of the tail, consists of a strong spine with a swollen base, in which is situated a pair of poison-glands with ducts opening terminally. The body is markedly segmented. The cephalothorax carries all the true appendages, and is covered dorsally by a shield, or carapace, on which are situated the eyes, generally one pair in the centre, and it may be two or even five lateral eyes on each anterior corner. The cheliceræ are short and pincer-like, the second pair of appendages, or pedipalps, resembling the claws of a lobster; the next four pairs of appendages are crawling legs. The mouth is very small, situated deeply between the pedipalps. The abdomen is very long, distinctly segmented, and composed of two portions; the anterior, composed of seven segments, bears the breathing-slits (stigmata), opening into a set of gills called lung-books. The posterior portion of the abdomen consists of five segments and a curved spine-like tail bearing the sting at its apex. When in action the tail is raised and bent forward over the back. Scorpions are viviparous and nocturnal in their habits.

Scorpions are grouped into seven families, of which the most important—the *Buthidæ*—contains 300 species. This genus is found in all parts of the tropics, and embraces the black scorpion (*Euscorpius italicus*), which is popularly supposed to be the most venomous.

Order iv.—THE ARANEIDA (SPIDERS)

The Araneida form a very large order. The body is composed of a chitinized cephalothorax carrying the true appendages, and a soft bulky abdomen attached to the former by a short stalk. The dorsal surface of the cephalothorax is covered by a carapace bearing the eyes, usually eight in number and arranged in two rows. The cheliceræ, or first pair of appendages, are the poison-fangs, with which spiders kill their prey; the second pair of appendages, or pedipalps, resemble the legs, except that the basal segment is produced to form a maxillary process. In the male the terminal segment is swollen and is used for impregnating the female; there are four pairs of legs, each consisting of seven segments ending in two or three claws. The abdomen is globular and is generally unsegmented. In front of the anus are situated three pairs of spinnerets, or spinning glands. The breathing organs open on the ventral surface of

Digitized by Google

the abdomen and consist of tracheæ or "lung-books." The mouth is a minute opening behind the cheliceræ, and the food consists of insects, which are sucked dry. The female greatly exceeds the male in size, and produces batches of eggs enveloped in a cocoon.

The venom of some spiders is particularly poisonous, and may be fatal to man; especially is this the case in the species known as *Latrodectus formidabilis*, which is found in Chile, and *L. scelio*, in New Zealand. A third species, *L. mactans*, has a bad reputation in Central and South America; a fourth, known as "Malmignatte" (*L. 13-guttatus*), is considered a dangerous species in Southern Europe. The poisonous extract of these spiders produces convulsions and death when inoculated into rabbits and rats, though harmless when given by the mouth.

Class III.—INSECTA

The Insecta are easily distinguished from the other arthropods by the division of their body into head, thorax, and abdomen, by the presence of three pairs of legs situated on the thorax, and of one pair of antennæ on the head.

The head is a chitinous capsule, sharply differentiated from the thorax, and contains, besides muscles, a supra-œsophageal ganglion and the pharynx; the appendages are sensory and feeding organs. The eyes are situated at the side of the head; on the under-surface is the mouth, guarded by the mouth-appendages; above it is a structure known as the *clypeus*. The mouth-parts consist, in their simplest form, of (1) median upper lip or *labrum*, (2) a pair of upper jaws or *mandibles*, (3) a pair of lower jaws or *maxillæ* bearing two accessory jointed appendages or maxillary palps, (4) a median lower lip or *labium* which may also bear palps. These mouth-parts vary in their arrangements in different insects. When the food is solid the mouth-parts assume the form of sharp, cutting plates. Those insects which live on liquid food have their mouth-parts adapted for sucking, the various parts being modified to form a tube or *proboscis*, through which liquid can be drawn. Those which live on blood have the labrum or upper lip projecting beyond the clypeus to form a long style, known as the *epipharynx*, and on the floor of the mouth there is a similar process, known as the *hypopharynx*, into which the salivary ducts open. Other structures on the head are *ocelli*, or simple eyes, which when present are usually three in number. The antennæ are placed between the eyes, and are usually elongated, flexible, and segmented; they often differ in the sexes of the same species; in function they are tactile, olfactory and, it may be, auditory.

The thorax and its appendages.—The thorax is composed of three segments, more or less marked off from one another—(1) the prothorax or first thoracic segment, (2) the mesothorax or second thoracic segment, and (3) the metathorax or third thoracic segment. Each of these segments has a corresponding pair of jointed legs, which are situated on the ventral surface. The wings are appendages of the thorax; in the typical adult insect there are two pairs, one attached to the meso- and the other to the metathorax; but in the Diptera, or true flies, only the anterior pair are present, while the posterior are represented by rudiments called *halteres*, or balancers; in other species the wings are absent. The wings are really outgrowths of the integument, stiffened and supported by a framework of veins, tubes of chitin containing air and, in their developmental stages, blood; they may carry hairs of several kinds, and scales. The thorax contains various viscera, the

Digitized by Google

gullet, salivary glands, ganglia of the ventral nerve cord, and the primitive blood-vascular system.

The legs differ considerably, being adapted to the particular mode of life of the various insects. Typically they consist of three pairs, one to each segment. Each leg consists of a coxa articulated to the thorax, a short trochanter, a femur and tibia both of considerable length, and a tarsus generally consisting of five pieces, the last of which ends in a pair of hook-like claws, sometimes in a single one, or *pulvillus*.

The respiratory system is represented by tracheæ, or air-tubes, which open to the outer air by oval pores, or *stigmata*, and are intersegmental in position. There are commonly ten pairs, occasionally fewer. The main tracheal branches unite to form a pair of trunks which run longitudinally along each side of the body, and communicating by transverse branches; they are kept from collapsing by spiral threads of chitin.

In aquatic larvæ this system is closed; breathing is then carried on through the skin, or by means of leaf-like processes filled with tracheal tubes, and known as tracheal gills.

The abdomen.—The abdominal segments are generally clearly marked and rarely bear appendages; more usually they are provided with hairs. The posterior segments of the female are generally modified to form an ovipositor.

The alimentary canal runs longitudinally throughout the body and opens posteriorly upon the last abdominal segment; in structure it varies considerably. In most insects the pharynx is modified by muscular attachments to form a suction pump, and the œsophagus is provided with crops or food-reservoirs. The stomach and intestine are situated within the abdomen, together with the reproductive organs. The rectum is provided with symmetrical glands known as rectal glands. Attached to the alimentary canal at the posterior end of the pharynx are three or four pairs of white tubules known as hepatic diverticula, which secrete a digestive fluid; and at the posterior end of the stomach, or mesenteron, is a series of fine, long, blind tubes, 60–80 in number, arranged in six bundles, and opening at the anterior end of the intestine; they are known as the Malpighian excretory tubules.

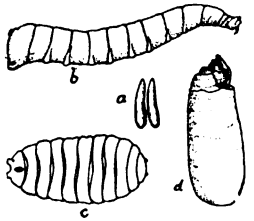


Fig. 358.—Life-history of Musca domestica.

a, Eggs; *b*, larva; *c*, pupa; *d*, empty puparium.

Reproduction.—The sexes are separate, the male being distinguished from the female by its smaller size and the character of its antennæ, and very often by its different mode of life. The male is parasitic on plants, while the female feeds on animal blood or tissues. *Parthenogenesis*, or reproduction by unfertilized eggs, is common. Certain species are viviparous. The egg, as a rule, contains much food material. In some cases the eggs are laid in water; the young are aquatic organisms and differ markedly in appearance and mode of life from the adults, and are then known as larvæ. The full-grown larva undergoes a resting stage known as the pupa, from which the adult organism, or imago, emerges. An insect which passes through all stages in the course of its development is said to show *complete metamorphosis* (Fig. 358); while others, in which the young when born resemble their parents to a certain extent, and become adult by a series of moults, are said to show *incomplete metamorphosis*.

Digitized by Google

Order i.—THE DIPTERA (Figs. 359-370)

Flies possess only an anterior pair of membranous wings, the posterior pair being represented by halteres. The mouth-parts are adapted for sucking or piercing. The number of visible abdominal segments varies between

Fig. 359.—Musca domestica, ♀. × 3 diam.

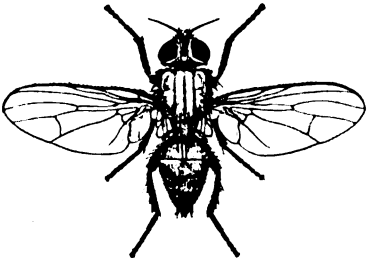


Fig. 360.—Fannia canicularis, ♀. × 4 diam.

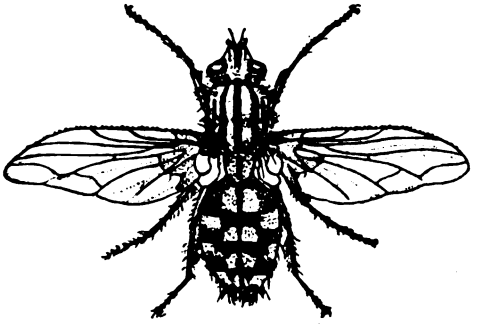


Fig. 361.—Sarcophaga carnaria. × 2 diam. (*After Brumpt.*)

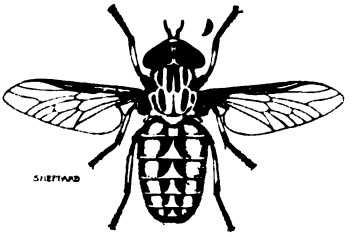


Fig. 362.—Tabanus ustus, ♂. Nat. size. (*Partly after Austen; by permission of Trustees of Brit. Mus.*)

Fig. 363.—Chrysops longicornis, ♀. × 2½ diam. (*Partly after Austen; by permission of Trustees of Brit. Mus.*)

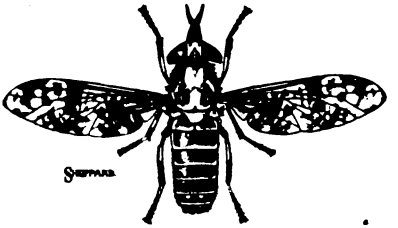


Fig. 364.—Hæmatopota, ♀. × 2½ diam. (*Partly after Austen; by permission of Trustees of Brit. Mus.*)

four and nine. The Diptera include the *Muscoidea*—that is, the houseflies, *Musca* and *Fannia*—*Calliphora*, the bluebottle, and *Sarcophaga*; *Auchmeromyia*, the Congo floor-maggot; *Cordylobia*, the Tumbu fly; the biting flies—

Digitized by Google

Tabanus, Chrysops, Hæmatopota, Pangonia; Stomoxys or stable fly, as well as *Hæmatobia* and *Lyperosia;* the tse-tse flies or *Glossinæ;* the mosquitoes or *Culicinæ;* the sandflies or *Psychodidæ,* including *Culicoides* and *Simulium.*

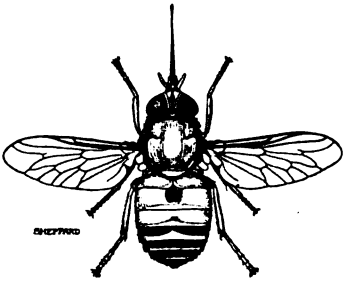


Fig. 365.—Pangonia rüppellii, ♀. × 1½ diam.
(Partly after Austen; by permission of Trustees of Brit. Mus.)

Fig. 366.—Stomoxys calcitrans. × 3 diam.

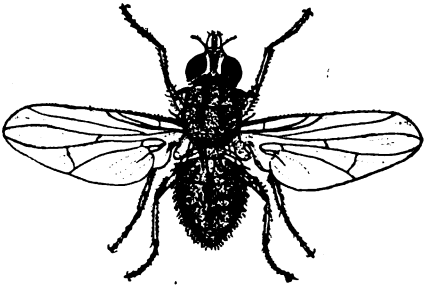


Fig. 367.—Lyperosia irritans. × 7 diam.

Fig. 368.—Simulium reptans. × 10 diam.

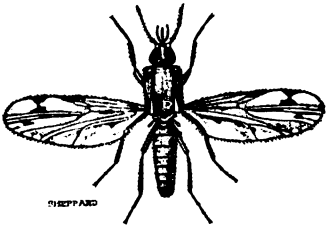


Fig. 369.—Culicoides, ♀. × 20 diam.

Fig. 370.—Hippobosca maculata. × 2 diam.

They also embrace the partially parasitic species—the *Œstridæ* or bot flies; *Hypoderma,* in mammals; the *Dermatobia,* or "Macaw-worm," in man; the *Hippoboscidæ* and *Nycteribiidæ,* parasitic on mammals, including *Melophagus,* the "sheep-tick."

Digitized by Google

Order ii.—THE ANOPLURA

Lice are small, flattened, thin-skinned insects without wings, with mouth-parts adapted for sucking, indistinctly segmented thorax, and having an incomplete metamorphosis. The number of abdominal segments ranges from six to nine, the last of which is bilobed. The abdomen of the male ends bluntly and bears a spine-like penis; the spiracles are very prominently situated on the sides of the abdominal segment. The eggs or nits adhere to the hairs of the host, and the newly-hatched young are small editions of their parents. The species which is parasitic on man is known as *Pediculus humanus*, of which there are two varieties, the head louse, *P. humanus capitis*, and the body louse, *P. humanus corporis*; some regard them, indeed, as forming but one species. (Fig. 371.) The third species is *Phthirus pubis*, the "crab louse," which lives in the genital and inguinal regions. It is distinguished from other lice by its broad flat body and by a line of three spiracles situated on each side of the second abdominal segment. The abdomen, of six segments, is festooned. The first pair of legs are more slender than

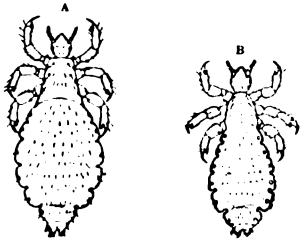


Fig. 371.—Pediculus. × 5 diam. (*After Bruce Cummings; by permission of Trustees of Brit. Mus.*)

A, Pediculus humanus, ♀.
B, P. humanus var. capitis, ♀.

Fig. 372. — Phthirus pubis, ♀, showing contained ovum. × 12 diam. (*Microphoto: Dr. J. Bell.*)

the other two; the second and third have massive talon-like claws, the thumbs of the tibiæ being prominent. The phthirus, when adult, clings to two approximated hairs, generally about 2 mm. apart, the span between the hind legs being about that distance. The young crab louse passes through three moults before attaining maturity. The life-cycle is complete in 27 days. When removed from man they die in 42 hours. Infestation with the crab louse occurs most frequently during coitus. (Fig. 372.)

In *P. capitis* and *corporis* the life-history is similar. The eggs hatch in from eight days at 32° C. to five weeks at a lower temperature, and the young louse begins to suck blood at once. It differs from the adult only in having antennæ composed of three joints instead of five. The immature louse moults three times before becoming mature; the final moult into the adult form takes place twelve days after hatching. Each adult female louse lays 8–12 eggs every day. The total life-span of such an individual is from four to six weeks. These insects cannot live for any length of time upon discarded clothing. Under experimental conditions they live longer apart from the body at low temperatures; at 40° C. they survive twelve hours, and at 5° C. ten days.

Infestation occurs through contact or close association with verminous

Digitized by Google

persons; their spread is greatly favoured when men sleep huddled together. Prevention consists in personal cleanliness, *removal* of hair, and frequent change of clothing.

For the destruction of lice in clothing on a large scale the most efficient method consists in the application of dry or moist heat. Both lice and nits are destroyed by a moderate degree of dry heat, 55° C. for 5 minutes, 65–70° C. for 1 minute. For practical purposes clothes should be exposed to 70° C. for 30 minutes. Disinfestation is best effected in hot-air huts. These measures may be supplemented by insecticide solutions, of which a 5-per-cent. crude carbolic solution containing soap is about the best, and may be used for leather and articles of clothing liable to be injured by heat. As a louse preventive, crude unoxidized naphthaline powder, as effective as N.C.I. and cheaper, may be dusted into the seams and renewed twice a week. Nearly all forms of treatment designed to kill lice upon the person aim at destroying the adult and immature insects, but do not destroy the nits or eggs. Chloroform water (5 : 1,000) rubbed on the infected scalp or body quickly stupefies all the living lice and renders their removal easy, but leaves nits unaffected. The removal of nits from the hair is facilitated by vinegar or acetic acid (10 per cent.).

Apart from their unpleasant habits, lice are of medical interest since they act as intermediary hosts or transmitters in relapsing fever, typhus, trench fever, and possibly other diseases as well.

Order iii.—THE HEMIPTERA

Bugs have two pairs of wings; both pairs may be membranous, or the front pair may have the basal half thickened to form a wing-sheath. The mouth-parts are adapted for sucking and piercing. Metamorphosis is incomplete. This order includes a number of plant bugs and the Cimicidæ or *bed bugs*, which are temporary ectoparasites on man, and in which the wings are rudimentary. The mouth-parts are characteristic; the labrum forms a segmented proboscis which, in repose, is bent under the head; there are no palps. The mandibles and maxillæ are provided with bristles near the tip, and it is with these that the bug obtains blood. The former are grooved along their opposed surfaces to form two channels, one for the saliva which is secreted, while the blood is haustellated along the other. The three thoracic segments are distinct; the prothorax is free and the mesothorax produced posteriorly to form a scutellcm. The abdomen is flattened dorso-ventrally. The odour emitted by bugs is secreted by certain glands which open on the sternum of the last thoracic segment. The sexes are separate, the male being distinguished from the female by the more elongated abdomen and by a notch on the fourth segment of the latter known as the organ of Berlese. The species parasitic on man are *Cimex lectularius*, the bed bug of Europe, and *C. hemipterus* (*rotundatus*), the bug of warm countries, which can be distinguished by its more elongated, narrower abdomen and by the greater dorsal convexity of the pronotum; this is the species which, according to Patton, is the intermediary host of the parasite of kala-azar. (Figs, 373, 374.) In West Africa a third species, *C. boueti*, also infests man. The European species is known to carry the spirochæte of relapsing fever. During the day the insect hides in a crevice, and at night sallies forth to suck blood.

The eggs are white and oval, cohering together in clumps; each egg has a lid through which the larva emerges, resembling its parents in general

Digitized by Google

appearance, but white in colour, and having no elytra or rudimentary wings.

The most effective method of destroying bed bugs in a building is fumigation with sulphur or, better still, with hydrocyanic acid gas; the latter, being dangerous, can only be carried out by some skilled person. For articles of furniture which cannot be subjected to boiling water an emulsion of petroleum made up with 3 parts soap to 15 of hot water, to which, while still hot, 70–100 parts of oil are added, should be forced into all cracks and crevices with a brush.

The family of *Reduviidæ*, large, active, rapacious land bugs, are particularly numerous in the tropics; several species are found in houses and attack man at night. *Conorhinus megistus*, a large black bug with numerous red markings, is known as the "barbeiro" in Brazil, and is the intermediary of the trypanosome of Chagas' disease (*T. cruzi*). (Fig. 375.)

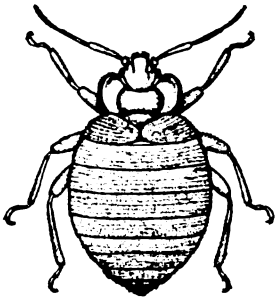


Fig. 373.—Cimex lectularius. × 7 diam.

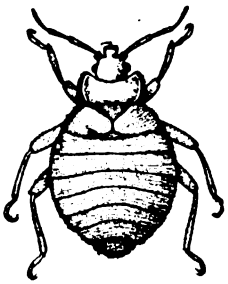


Fig. 374. — Cimex hemipterus (rotundatus). × 6 diam.

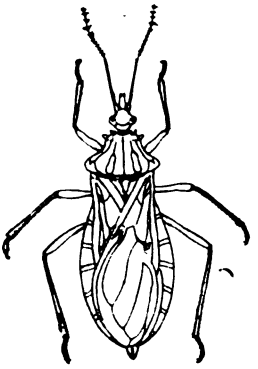


Fig. 375.—Conorhinus. Nat. size.

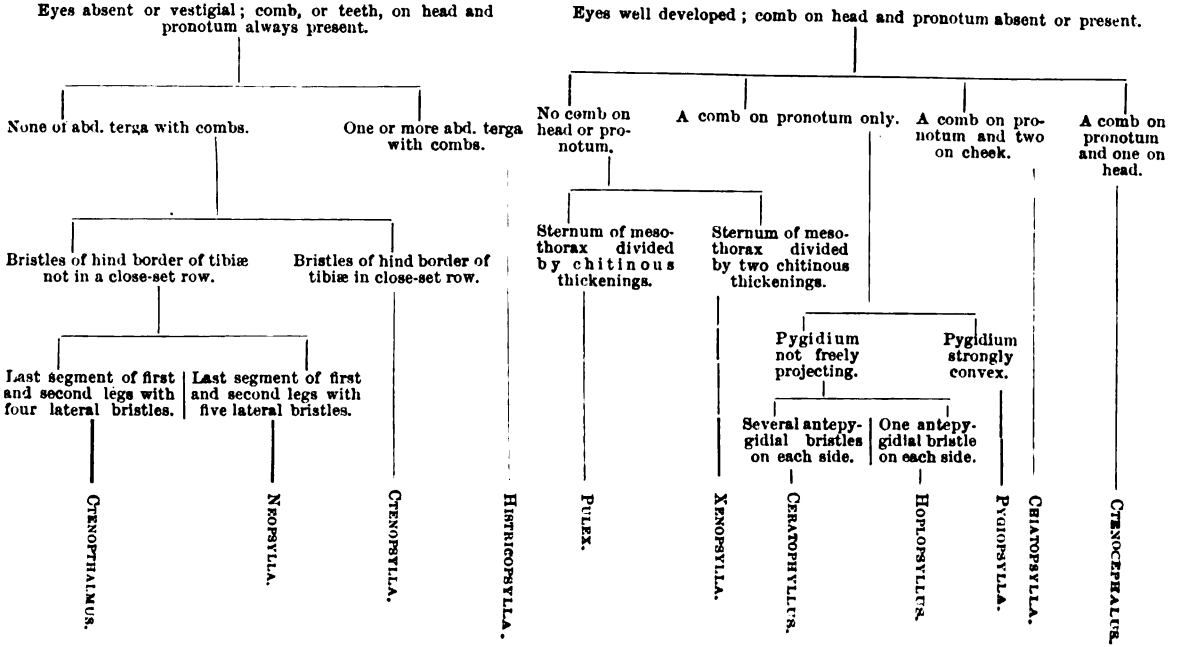
Order iv.—THE SIPHONAPTERA

Fleas are small insects with a laterally compressed body. They are wingless, and their mouth-parts are adapted for piercing and sucking. Some suck blood indiscriminately, but the majority restrict themselves to one definite host and are active ectoparasites of mammals and birds. In one family, *Sarcopsyllidæ*, or "chiggers," the females eventually attach themselves to their host as fixed parasites, embedding themselves in the skin when pregnant. The external structure of a flea is composed of head, thorax, and abdomen.

The *head* is small compared with the abdomen, and is conical in shape, with sometimes a comb of teeth on the cheek, or on the lower edge of the head. Eyes may or may not be present. The head is provided with short antennæ lodged in definite grooves. The mouth is furnished with appendages, maxillæ and palps, which conceal the other parts. The *thorax* is composed of three segments, which are quite independent. Each consists of a dorsal arc carrying one or more belts of bristles. In some species the pronotum, or tergum of the first thoracic segment, carries a comb on its posterior border. The three pairs of legs are composed of a number of segments,

Digitized by Google

SYNOPSIS OF FLEAS.—I. FAMILY PULICIDÆ


Eyes absent or vestigial; comb, or teeth, on head and pronotum always present.
Eyes well developed; comb on head and pronotum absent or present.
None of abd. terga with combs.
One or more abd. terga with combs.
No comb on head or pronotum.
A comb on pronotum only.
A comb on pronotum and two on cheek.
A comb on pronotum and one on head.
Bristles of hind border of tibiæ not in a close-set row.
Bristles of hind border of tibiæ in close-set row.
Sternum of mesothorax divided by chitinous thickenings.
Sternum of mesothorax divided by two chitinous thickenings.
Last segment of first and second legs with four lateral bristles.
Last segment of first and second legs with five lateral bristles.
Pygidium not freely projecting.
Pygidium strongly convex.
Several antepygidial bristles on each side.
One antepygidial bristle on each side.
CTENOPHTHALMUS.
NEOPSYLLA.
CTENOPSYLLA.
HISTRICOPSYLLA.
PULEX.
XENOPSYLLA.
CERATOPHYLLUS.
HOPLOPSYLLUS.
PYGIOPSYLLA.
CHIATOPSYLLA.
CTENOCEPHALUS.

II. FAMILY SARCOPSYLLIDÆ (DERMATOPHILIDÆ)

1. Hind coxæ without a patch of spines on the inner side = *Dermatophyllus*. 2. Hind coxæ with a patch of spines on the inner side = *Echidnophaga*

Digitized by Google

the coxa being especially long and broad. The number and character of the bristles of the joints of the legs are used for distinguishing species. The *abdomen* is composed of ten segments; on the ninth the tergum is in a great part occupied by a pitted sensory plate called the pygidium. In the male the sides of the tergum form large claspers. Large bristles project over and beyond the pygidium on the seventh segment, and are known as antepygidial bristles. There is a large and complex penis.

The female flea is larger than the male. The curved receptaculum seminis is a conspicuous object in the female.

The eggs are dropped by the female casually, and hatch in three or four days in summer time.

The larva lives in dust, is an active footless maggot, of a whitish colour, and is sparsely hairy. (Fig. 376.) When full grown it spins a cocoon and

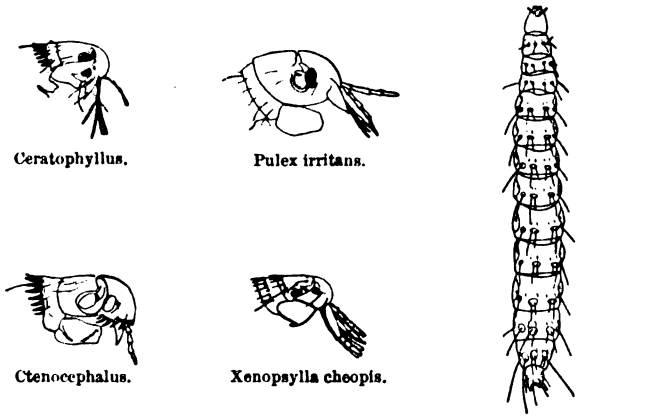


Fig. 376.—Heads and larva of fleas. (*After Bacot and Ridgway, "Parasitology."*)

pupates. The duration of the pupal stage depends on the temperature. The pupæ are similar to the adult and are encased in a cocoon.

Fleas act as mechanical carriers of disease, and also as intermediary hosts of parasites. The common dog-flea, and rat-fleas, harbour the cysticercus of certain tapeworms (*Dipylidium caninum*), and are said to transmit the *Leishmania donovani* in Italy; but their most important rôle is as carriers of the plague bacillus from rats to man.

The presence of fleas in houses is chiefly due to want of cleanliness, especially the accumulation of dust, the proximity to hen-runs or stables, and free access of flea carriers—cats, dogs, rats and mice.

To rid cats and dogs of these insects they should be washed with carbolic soap or a strong lather of "vermijelli." Cats that object to water may be powdered with naphthaline or dusted with pyrethrum. The floors of the house should be washed with a solution of naphthaline or benzene. An emulsion of petroleum which will kill fleas when diluted with water, 1 : 20 or more, may be made from soft soap and ordinary petroleum, 3 parts

Digitized by Google

of soap being melted by heat in 15 of water, and 70–100 parts of oil added, while still hot, with much shaking and stirring. The final mixture should be white and creamy.

Sub-class Myriapoda

This group includes the centipedes, in which some species have long poison-claws capable of inflicting serious injury. In certain cases they have been found in the nasal cavities and the ears, and have actually been ingested into the alimentary canal, where they are able to accommodate themselves and live for a considerable period and give rise to serious symptoms. The body is elongated and composed of a head and numerous segments, each with a pair of appendages. The mouth-part consists of a pair of many-jointed antennæ, a pair of mandibles, and two pairs of maxillæ. Breathing is performed by tracheæ. (Fig. 377.)

Fig. 377. Lithobius forficatus. Nat. size. (*After Brumpt.*)

The Myriapoda are classified into four orders, of which the *Chilopoda*, or centipedes, and the *Diplopoda*, or millipedes, are the most important. The female centipede, as a rule, produces eggs; the newly-hatched young resemble their parents. The injury inflicted by the poison-claws of the large centipedes is very painful, and causes numbness and tingling which may last for hours. Considerable local swelling ensues, and this may go on to suppuration. General symptoms such as sickness and faintness may continue for some time afterwards. The best-known poisonous species in the tropics is *Scolopendra cingulata*.

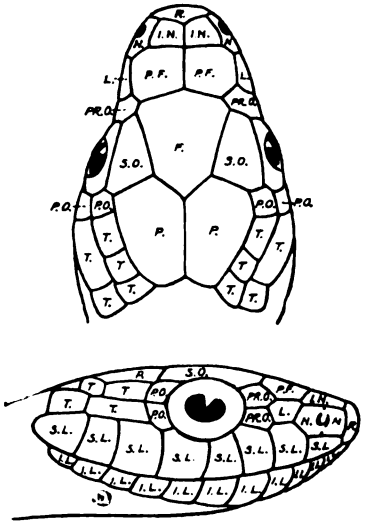


Fig. 378.—Diagram of scales on snake's head. (*Partly after Alcock.*)

CLASSIFICATION OF SNAKES (ORDER *OPHIDIA*)

The snakes form an order of the class *Reptilia*, distinguished by a limbless body encased in a horny integument. Their eyes are unprovided with eyelids; the head has no tympanic cavity or external auditory meatus. The cloaca is transversely situated, and in the male the penis is paired. Locomotion is effected by the flexibility of the ribs, in the absence of limbs. The tongue is bifid, protractile, and ensheathed.

Recognition and classification of snakes is effected by a study of the arrangement of the scales covering the head, the formation of the skull, and dentition. On the ventral surface of the body the large overlapping scales are known as *shields*. The arrangement of the scales on the head is shown in the accompanying diagram

Digitized by Google

(Fig. 378). About 1,700 species of snakes are known, of which 300 may be classified as venomous, and in most of these the anterior teeth are grooved and channelled so as to form poison-fangs. There are seven non-poisonous families of snakes, including the blindworm snake (*Typhlopidæ*) and the pythons (*Boiidæ*). The two families to which the poisonous genera or *Thanatophidia* belong are the *Colubridæ* and the *Viperidæ*.

A few vipers may resemble colubrines, but the two families are separable upon the osteological characters of the skull; in the Viperidæ the maxilla is short and lies obliquely, while in the Colubridæ it is of considerable length and lies horizontally. (Fig. 379.) The diamond-shaped head and the narrow neck and the short, sharp, stumpy tail are other familiar viperine characters.

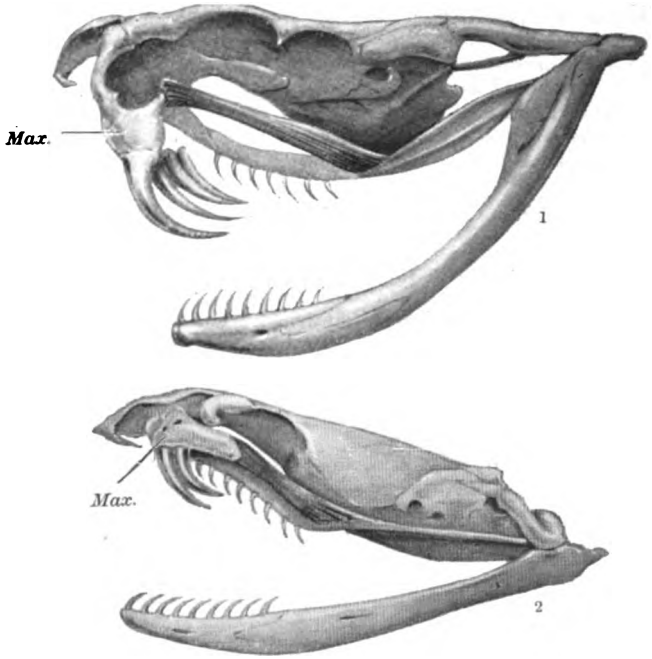


Fig. 379.—Snake skulls. Nat. size. (*From specimens in the London School of Tropical Medicine.*)

1, Viperine skull = Crotalus horridus; 2, colubrine skull = Elaps marcgravii. *Max.* = maxilla.

COLUBRIDÆ

The Colubridæ form a large family, numbering nearly 1,300 species, and are divisible into three sections according to the arrangement of the teeth, namely, the *Aglypha*, the *Opisthoglypha*, and the *Proteroglypha*.

(*a*) **Aglypha.**—The maxilla bears numerous teeth, none of which are grooved. All these species, more than 700 in number, are *harmless*, for, although possessing glandular structures homologous with the poison-glands of other Thanatophidia, the secretion contains but a small amount of toxin and cannot be injected into the wound.

Digitized by Google

(*b*) **Opisthoglypha** (about 300 species).—The maxilla is elongated and bears many teeth, of which one or more of the posterior set are openly grooved anteriorly. Although these snakes secrete a toxin from their salivary glands and have the means provided for instilling the poison, they are not definitely known to be venomous to man.

(*c*) **Proteroglypha.**—All the colubrines of this group are poisonous; their maxilla is of moderate length, and one or more of the anterior teeth are hypertrophied to form poison-fangs, which are so deeply grooved and folded as to appear tubular. The proteroglyphs are divided into two sub-families, the *Elapinæ*, or land colubrines, and *Hydrophinæ*, or sea-snakes.

(1) *Elapinæ* comprise about 140 species, of which nearly one-half belong to the Australian region, while the remainder are spread throughout the tropics of both hemispheres.

(2) The *Hydrophinæ*, or poisonous sea-snakes, have the posterior portion of the tail so specialized as to form a sort of paddle. They number 50–60 species altogether, which are found in the Indian and Pacific Oceans. Although when unmolested they are unaggressive and harmless, their venom, when tested under artificial conditions, is known to be extremely toxic.

VIPERIDÆ

About 110 species belong to this family; all are more or less poisonous and possess large poison-fangs. The external "viperine characters" are not an infallible guide in distinguishing this family from the colubrines, as in the latter there are certain exceptions. The most distinctive mark is the short, almost perpendicular maxilla, while the transpalatine bone lies almost at a right angle, instead of in the same plane, as in the colubrines. The Viperidæ are divisible into two sub-families, the *Viperinæ* and the *Crotalinæ*.

(1) **Viperinæ.**—These comprise about 45 species and have a wide range in Asia, Africa, and Europe.

(2) The **Crotalinæ**, or pit vipers, comprise the rattlesnakes of America. They are distinguished by the presence of a sensory uveal pit situated between the eye and the nostril.

SYNOPSIS

The classification of snakes is best set out in the following synopsis, based upon Alcock's scheme, originally published in Daniels' "Tropical Medicine and Hygiene," Part II.

No transpalatine bone; body covered with hard "cycloid" scales of uniform size. Worm-like snakes with obscure eyes lying beneath the head-shields 1

Transpalatine bone present; scales and eyes of ordinary form 2

1. No squamosal bone; pterygoid not extending to quadrate or mandible; coronoid bone present 3

3. Maxilla placed transversely, with a few teeth; mandible toothless . . . . . *Typhlopida*

Maxilla toothless, not transverse; mandible with teeth . . . . . *Glauconiida*

2. Coronoid bone present; ventral shields either moderately large or quite small. 4

Digitized by Google

Coronoid bone absent; ventral shields, except in aquatic species, very large 5
4. Squamosal bone present; concealed vestiges of hind limbs 6
No squamosal bone; no vestiges of hind limbs . . . 7
6. Squamosal large; ventral shields usually moderately large. . . . . *Boiidæ*
Squamosal small; ventral shields hardly at all enlarged . . . . . *Ilysiidæ*
(South-Eastern Asia and Tropical South America)
7. Burrowing snakes, restricted to Ceylon and Southern India; ventral shields small . . . . . *Uropeltidæ*
5. Maxilla horizontal. 8
Maxilla short, not horizontal, vertically erectile . . *Viperidæ*
8. Pterygoid bone reaching quadrate or mandible with a mental groove 9
Pterygoid not reaching quadrate or mandible; no mental groove . . . . . *Amblycephalidæ*
(South-Eastern Asia and South America)
9. Teeth in premaxilla . . . . . *Xenopeltidæ*
(South-Eastern Asia)
No teeth in premaxilla . . . . . *Colubridæ*
Colubridæ—(i.) None of the maxillary teeth grooved . *Aglypha*
(ii.) Some of the posterior maxillary teeth enlarged and grooved . . . *Opisthoglypha*
(iii.) Anterior tooth in the maxilla enlarged and grooved . . . *Proteroglypha*
Proteroglyph Colubridæ, divisible into—
(*a*) *Hydrophinæ:* tail strongly compressed and paddle-like—sea snakes.
(*b*) *Elapinæ:* tail cylindrical—land snakes.

Synopsis of Hydrophinæ

Ventral shields small or altogether undifferentiated . . . 1
Ventral shields large 2
1. Mental shield triangular, not concealed in groove . . . 3
Mental shield narrow, partly concealed in deep groove in chin . . . . . *Enhydrina*
(Persian Gulf to New Guinea)
2. Nostrils on top of the snout (as usual in this subfamily) . . . . . *Æpysurus*
(Java to New Caledonia)
Nostrils lateral (as in most land snakes) . . . *Platurus*
(India to Fiji and New Zealand)
3. No differentiated ventral shields 4
Small ventral shields present, at least in part of the body 5
4. Lateral scales of the lower rows enlarged . . . *Enhydris*
(Bay of Bengal to New Guinea and China)
Lateral scales of the lower rows not enlarged . . *Hydrus*
(East Africa to Panama)

Digitized by Google

5. Only the poison-fangs grooved . . . . . *Hydrophis*
(Persian Gulf to North Australia and China)
All the maxillary teeth and sometimes also the anterior mandibular teeth grooved . . . . . *Distira*
(Persian Gulf to Japan and New Caledonia)

Synopsis of Genera of Elapinæ

i. *African Elapinæ*

Tail more than $\frac{1}{7}$ total length 1
Tail less than $\frac{1}{9}$ total length 2
1. Maxilla of ordinary form 3
Maxilla curved upwards with a strong spur at its posterior end . . . . . *Dendraspis*
3. Scales disposed very obliquely 4
Scales not remarkably oblique 5
4. Scales smooth; neck in most species dilatable . . *Naja*
Scales strongly keeled . . . . . *Sepedon*
5. No teeth in the maxilla except the poison-fangs; tail short . . . . . *Walterinnesia*
Three or four teeth in the maxilla besides the poison-fangs; tail long . . . . . *Boulengerina*
2. Rostral shield normal 6
Rostral shield very large, detached at sides . . . *Aspidelaps*
6. Poison-fangs grooved as usual; no longitudinal vertebral stripe . . . . . *Elapechis*
Poison-fangs not grooved; often a bright longitudinal vertebral stripe . . . . . *Homoroelaps*

ii. *Asiatic Elapinæ*

1. A row of enlarged scales along the middle line of back *Bungarus*
No mid-dorsal line of enlarged scales 2
2. Large snakes, not brilliantly coloured; neck dilatable . . *Naja*
Long slender snakes, often with stripes or bands, and usually showing some red in their colouring; neck not dilatable 3
3. From one to three small teeth in the maxilla behind the poison-fangs . . . . . *Hemibungarus*
No teeth in the maxilla except the poison-fangs . . . 4
4. Poison-gland situated in the temporal region as usual . *Callophis*
Poison-gland having the form of a long slender cord extending far along the body . . . . . *Doliophis*

iii. *Australian Elapinæ*

These are very numerous and are often separable only by slight differences into—
Viper-like snakes . . . . . 1. (*Brachyaspis, Acanthrophis*)
Not viper-like in appearance . 2. (*Rhinoplocephalus, Pseudechis, etc.*)

iv. *American Elapinæ*

These include about 30 species all belonging to the genus ***Elaps***. They are generally bright-coloured species.

Digitized by Google

Synopsis of Viperidæ

A sensory uveal pit between the eye and the nostril . *Crotalidæ*
No uveal pit . . . . . *Viperinæ*

(*a*) synopsis of genera of viperinæ

Crown of the head with large symmetrical shields like a colubrine 1
Crown of the head with small scales only, or with small scales and some small shields 2
1. Numerous teeth in mandible; loreal shield present . . 3
Only two or three teeth in mandible; no loreal shield . *Atractaspis* (Africa, Arabia, and Persia)
3. Pupil round; scales on sides of body very oblique. . *Causus* (Africa)
Lateral scales not particularly oblique . . . . *Azemiops* (Upper Burma)
2. Scales on sides not smaller than those on back, their keels sharp, i.e. not serrated 4
Scales on sides smaller than those on back 5
4. Ventral shields of ordinary curved form 6
Ventral shields with a keel on either side . . *Eristicophis* (Baluchistan)
6. Nasal shield either touching rostral shield or separated by a naso-rostral shield . . . . . *Vipera* (Europe, Asia, and Africa)
Nasal shield separated from the rostral shield by small scales 7
7. A semilunar supranasal shield . . . . . *Bitis* (Africa and Arabia)
No supranasal shield . . . . . *Pseudocerastes* (Persia and Baluchistan)
5. Scales on the sides of the body with sharp keels; tail about $\frac{1}{6}$–$\frac{1}{4}$ of total length . . . . . *Atheris* (Africa)
Scales on sides of body with serrated keels; tail short . . 8
8. Ventral shields of ordinary curved form . . . *Echis* (Asia and Africa)
Ventral shields with keel on either side . . . *Cerastes* (Africa, Arabia, and Syria)

(*b*) synopsis of genera of crotalinæ

1. Tail ending in a rattle 1
Tail not ending in a rattle 2
1. Head with large symmetrical shields; small slender snakes . *Sistrurus* (North America)
Head with small scales alone, or with small scales and some small shields. Large bloated snakes as a rule . *Crotalus* (North and South America)
2. Head with large symmetrical shields . . . *Ancistrodon* (Asia and America)
Head with small scales alone, or with small scales and some small shields . . . . . *Lachesis*

Digitized by Google

APPENDIX III

LABORATORY METHODS AS APPLIED TO CLINICAL MEDICINE IN THE TROPICS

I.—CLEANING SLIDES AND COVER-SLIPS

NEW slides are suitable for making blood-films directly the superficial grease is removed by breathing on them and rubbing up with a clean handkerchief or gauze.

Slides which are dirty or have previously been used should be boiled in a soapy solution for about half an hour, then washed in several changes of water, and finally polished with old linen dipped in methylated spirit.

For finer work, dirty slides or cover-slips are boiled for half an hour in a mixture of—

Concentrated sulphuric acid	6 parts
Potassium bichromate	6 ,,
Water	100 ,,

They are then thoroughly washed in water, transferred to spirit, and dried as required.

II.—METHODS OF PREPARATION OF BLOOD-FILMS

THIN FILMS

Method i.—Take a droplet of blood, obtained by pricking the cleansed finger or ear-lobe, on the end of a slide. A second slide should be touched, about ¾ in. from the end, with the drop, and the blood allowed to run along the edge. The spreading slide should be pushed, at an angle of 45°,

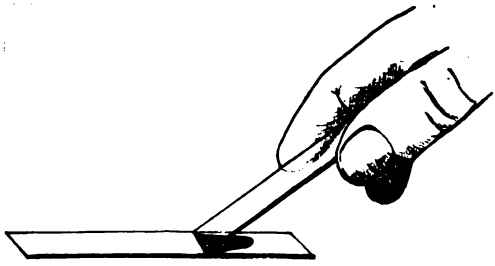


Fig. 380.—Method of spreading a blood-film.

to the opposite end of the horizontal one, leaving a thin and evenly-spread film, which should be allowed to dry. An angle of less than 45° makes a thinner, and one greater than this angle a thicker film. (Fig. 380.)

Method ii.—This is a quick and easy way of preparing blood-films

Digitized by Google

Prick the cleansed finger-pad or lobe of the ear, and express a droplet of blood. Take this up by touching it lightly with a clean glass slip about 1 in. from one end of the slip. Across the slip and on the blood lay the shaft of the needle—an ordinary straight, rather long sewing-needle (Fig. 381). Pause for several seconds until the blood has run out by capillarity between the needle and the slip; then, holding it by one end, push the needle over the face of the slip in the direction of the length of the latter, so as to spread the blood over the entire breadth of the middle third of the slip. The successful preparation should thin off at the margins and end of the film. The blood-cells should be arranged so as not to be superimposed one upon the other, and the leucocytes should be round and regular, and not distorted in any manner. The blood-platelets should be arranged in clumps or in strings (Fig. 382).

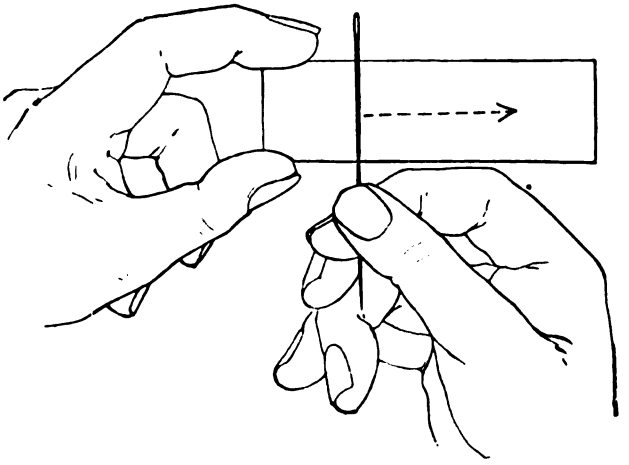


Fig. 381.—Another method of preparing blood-films.
("*Practitioner*," *March*, 1901.)

Films for making a differential count of cells should be prepared as in the first method, taking care to press unevenly upon the spreading slide, so as to obtain a wave-like film every quarter of an inch or so along the horizontal one. By these means the leucocytes collect along the edges of the waves, enabling the enumeration to be done much more easily and more rapidly. (Fig. 383.)

Thick Films

Ross's thick film consists of an evenly-spread smear of blood 5–7 mm. in diameter. After dehæmoglobinization with water it is dried in air and stained in the ordinary way. It has been found more advantageous to use a larger film, and it has been estimated that in this way the chances of finding malaria parasites and trypanosomes are increased by 50 per cent. (Fig. 384.)

A large drop of blood is taken on a slide and spread to about the size of a shilling. It should then be allowed to dry for at least one hour prior to staining, and should be carefully protected from dust during this period.

Digitized by Google

The slide is now covered with the following mixture, viz. solution A, Azure II, 1 : 1,000, in neutral distilled water; solution B, Eosine, 1 : 16,000, best kept as a 1-per-cent. solution; for use add 3 c.c. to 500 c.c. of neutral distilled water. Mix 1 c.c. of A with 9 c.c. of B just before using, as the mixture does not keep well. The watery solution both dehæmoglobinizes and stains the film at the same time. After the stain has acted for 30 minutes, wash the slide with *neutral* distilled water and allow it to dry, protected from dust.

Dilute Leishman or Giemsa stain (1 : 20) may also be used in the same manner.

There is considerable difficulty in differentiating the younger forms of benign tertian and quartan from subtertian malaria parasites, such details as

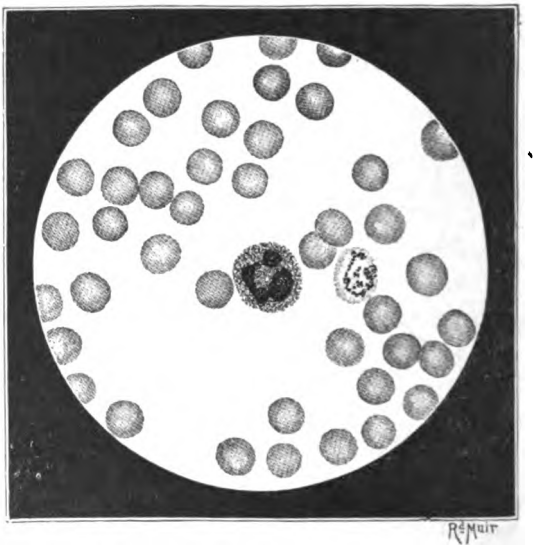


Fig. 382.—Showing the necessary disposition of blood-corpuscles in slides for examination for the plasmodium. To the right of the white blood-corpuscle in the centre of the field a red blood-corpuscle three-fourths filled with a tertian parasite is visible. (*Microphoto: Dr. Cosens.*)

Schüffner's dots being rendered invisible by this method. It is, however, very useful for demonstrating parasites in scanty infections, especially in the case of the gametocytes of benign tertian and the crescents of the subtertian. It is also useful for the demonstration of the spirochætes of relapsing fever when these, as is often the case, are extremely scanty.

Films for demonstration of microfilariæ.—An even larger-sized drop should be taken (20 c.mm.) and spread so as to occupy an area of ½ sq. in. on the slide. For this purpose the finger should be pricked with a broad-pointed needle and the under-surface dabbed with four good-sized drops. The film is allowed to dry, protected from dust (especially cotton fibres, which may simulate microfilariæ), dehæmoglobinized, and stained at the same time in a dilute watery solution of fuchsin (5 drops to 150 c.c. distilled water), then examined in a wet state under a low power of the microscope.

Digitized by Google

If permanent hæmatoxylin-stained preparations are required, after dehæmoglobinization, films must be fixed in alcohol and ether (equal parts), and stained with Delafield's hæmatoxylin for about 7 mins. They are then differentiated momentarily in acid alcohol, washed in tap-water till blue, dried, and mounted in Canada balsam. For *F. bancrofti* of the periodic variety the blood should be taken after 10 P.M., and for *L. loa* after 10 A.M.

Fluid Blood-Films

A small drop of blood should be taken upon a clean slide, inverted, and allowed to come into contact with a clean cover-slip upon a filter-paper.

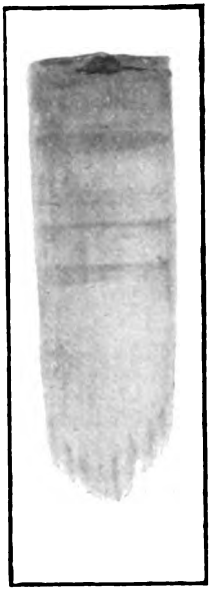


Fig. 383.—Successful thin blood-film. (*Orig.*)

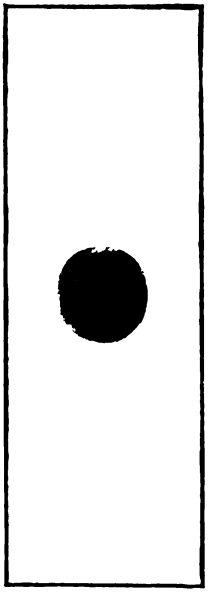


Fig. 384.—Thick blood-film preparation. (*Orig.*)

If no pressure is used the blood spreads out evenly, the corpuscles tending to congregate round the periphery while the centre remains clear. The preparation may then be ringed with vaseline and the blood-cells or contained parasites studied in the living state under a $\frac{1}{12}$-in. lens.

III.—STAINING OF BLOOD-FILMS FOR PROTOZOA AND FOR THE DIFFERENTIAL COUNT OF CELLS

Leishman's method.—For this method *no fixation is required.*

Preparation of stain from the powder.—Leishman's stain, 0·15 per cent., dissolved in methyl alcohol (acetone-free). The powder is placed in a glass mortar, a quantity of methyl alcohol added, and the powder ground down with a pestle until the alcohol is saturated. The yellow decanted off

Digitized by Google

into a clean bottle and a further fraction of methyl alcohol added to the residue in the mortar, which is again ground down until as much as possible is dissolved. This process is repeated until the whole of the powder is in solution, and sufficient methyl alcohol is added finally to the stain to make up the required volume.

Method of staining.—1. Select the most suitable part of the blood-film and place a grease pencil-mark on each side, about 1 in. apart—a method which in staining large batches of films results in great economy.

2. Cover the selected part with stain by means of a pipette, and leave for 30 secs.

3. Dilute the stain about 1 in 4 with distilled water, *which must not be acid in reaction* (fresh rain-water may be used), and allow to act for a further 5 mins. (*See* Tribondeau's test, p. 883.)

4. Wash off the stain with distilled water; place in a sloping position to drain, or dry with blotting-paper.

For permanent preparations Leishman-stained slides must *not* be mounted in Canada balsam, as they rapidly fade; they should be examined unmounted direct in cedar-wood oil, and the oil subsequently removed by means of xylol. (Fig. 385.)

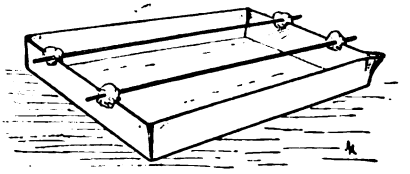


Fig. 385.—Trough for staining blood-films. (*A. Michieli, del.*)
Two glass rods affixed to a photographic developing dish with plasticine.

Giemsa's stain.—It is best to obtain the stain already prepared for use by Grübler. *The film must first be fixed* by placing in a mixture of equal parts of absolute alcohol and ether for 10–15 mins.

Method of staining.—1. The film should be covered with a 1 : 20 dilution of the stain (1 drop to 19 drops distilled water), which is allowed to act for 20–30 mins.

2. Wash off the stain with distilled water; place the slide in a sloping position to drain, or dry with blotting-paper.

Gauducheau's stain.—This stain has been used latterly as a substitute for those already mentioned. *No fixative is required.*

Composition:

A. Borrel's blue.
B. 1-per-cent. solution of methylene blue in 95-per-cent. alcohol.
C. 0·5-per-cent. solution of eosin in absolute alcohol.

Mix 6 c.c. of A with 18 c.c. of B; add 30 c.c. of C, followed by 140 c.c. of absolute alcohol.

Borrel's blue is prepared as follows: Some crystals of silver nitrate are dissolved in a minimum amount of water in a 100-c.c. flask. Fill up the flask with 10-per-cent. caustic soda solution. Allow precipitate of silver oxide to settle, and decant off supernatant fluid. Wash the precipitate with distilled water until all trace of alkali has disappeared. To the precipitate in the flask add about 100 c.c. of a saturated aqueous solution of

Digitized by Google

methylene blue. Allow to stand 3–4 weeks, shaking occasionally. The solution should then be filtered. The filtrate is known as Borrel's blue.

Method of staining.—1. Cover the preparation with stain and leave for 2–3 mins.

2. Dilute the stain with distilled water 1 : 5 and leave for a further 4–6 mins.

3. Wash off the stain with distilled water ; place slide in a sloping position to drain, or dry with blotting-paper.

The length of time of staining depends upon the activity of the stain and must be gauged for each batch.

Hæmatoxylin and eosin.—For studying the finer structure of the leucocytes, and especially the nuclear changes, blood-films should be stained by hæmatoxylin and eosin.

After fixation in alcohol and ether for 10 mins. the film should be stained with Delafield's hæmatoxylin for 7 mins. The stain should be well flushed off the film with a good flow of tap-water, and it should be left in a running stream of the same for an equal period in order to " blue " thoroughly. Whilst still wet it should be counterstained with a watery solution (5 per cent.) of eosin for 30 secs., after which it should be thoroughly rinsed in tap-water for another 3 mins. in order to differentiate the eosin.

The film should then be dried and examined in cedar-wood oil under the $\frac{1}{12}$-in. lens.

Method of staining the flagellated body in malaria.—A sheet of thick blotting-paper, having rows of oblong holes (1 in. by $\frac{3}{4}$ in.) cut in it, is prepared ; it is slightly but sufficiently moistened with water, and laid smoothly on a sheet of window-glass.

A patient in whose blood the crescent form of the parasite abounds is selected. His finger is pricked and a droplet of blood, the size of a large pin's head, is expressed. A clean microscope slide is then breathed on once, and the droplet of blood immediately taken up by lightly touching it with the centre of the breathed-on surface of the slip. The blood is now rapidly and somewhat unevenly spread out with the needle so as to cover an area of about $\frac{3}{4}$ in. by $\frac{1}{2}$ in. The slide is immediately inverted over one of the blotting-paper cells and pressed down sufficiently to secure thorough apposition of the slip to the paper, without, at the same time, bringing the blood into contact either with the moistened paper forming the wall, or with the glass forming the floor of what is now a very perfect moist chamber. The rest of the paper cells are rapidly covered with blood-charged slides prepared in the same way. In from a quarter to three-quarters of an hour the slides are removed and dried by gently warming them over the spirit-lamp—blood surface away from the flame. When dry the films are fixed with absolute alcohol, a few drops being poured on each. After ten minutes the alcohol is dried off, and a few drops of weak acetic acid (10–20 per cent.) are laid on the films and left there long enough thoroughly to dissolve out all the hæmoglobin. The slides are then washed in water and dried. They may now be stained with various reagents. Manson obtained the best results from weak carbol-fuchsin (20 per cent.) and prolonged staining. The stain is dropped on the slide and covered with a watch-glass ; after 6–8 hours it is washed off with water, the slide dried, and a cover-glass applied with xylol balsam. Very fine results may also be obtained by staining with dilute Giemsa, 1 : 20, for 24 hours, or even longer.

Tribondeau's hæmatoxylin test for reaction of distilled water.—Two drops of a saturated alcoholic solution of hæmatoxylin should be added to

Digitized by Google

a test-tube half filled with the water under examination. If the water be *neutral*, the purple colour of hæmatoxylin will develop in 2–4 mins.; if *alkaline*, the colour develops immediately; if *acid*, it is delayed. The addition of 1-per-cent. acid or alkali should be made until the colour appears in the prescribed time.

IV.—MEASUREMENT OF MICROSCOPIC OBJECTS

For this purpose an ocular micrometer and a stage micrometer are employed. Some ocular micrometers, such as those made by Leitz, are so arranged that they rest upon the diaphragm inside the ocular; other kinds are inserted into the ocular by a lateral opening, while in still other cases (Zeiss) an ocular is made specially for measuring. In measuring an object, the stage micrometer is placed upon the stage of the microscope, which is also provided with an ocular micrometer. The number of divisions of the ocular micrometer corresponding to one part of the stage micrometer should be ascertained.

The dimensions of the divisions on the stage micrometer being known, the size of the object which, with a given number of magnifications, will occupy one or more of the divisions on the ocular micrometer is easily calculated.

The following examples will render the process more intelligible:

1. With ocular 1 and the draw-tube pushed in, 5 divisions of the ocular micrometer correspond to one division on the stage micrometer. Each division in the stage micrometer used = $\frac{1}{20}$ mm. Thus, 5 divisions of the ocular micrometer = $\frac{1}{20}$ or 0·05 mm., and 1 division = 0·01 mm. If, then, any microscopic object, the diameter of which is to be measured with this magnification, occupies 4 divisions, the diameter of that object is 0·04 mm.

2. With Leitz objective 3, ocular 1, and the draw-tube drawn out, 40 divisions on the ocular micrometer correspond with 5 divisions of the stage micrometer; therefore 40 divisions = $\frac{5}{20}$ mm. = 0·25 mm., and 1 division of the ocular micrometer with this magnification = 0·0062 mm., 2 divisions = 0·0124 mm., and so on.

3. With Leitz objective 7, ocular 1, and the draw-tube pushed in, 30 divisions of ocular micrometer = 1 division stage micrometer; therefore 30 divisions = 0·05 mm., 1 division = $\frac{0·05}{30}$ = 0·0017 mm. or 17 μ.

4. With Leitz objective 7 and ocular 1, and the draw-tube out, 40 divisions on the ocular micrometer = 1 division on the stage micrometer; therefore 40 divisions = 0·05 mm. and 1 division = $\frac{0·05}{40}$ = 0·0012 mm. or 12 μ.

It is sometimes difficult, especially with low magnification, to count the fine divisions on the ocular micrometer. This is rendered easier by noting the longer lines marking every fifth or tenth division.

In making series of microscopic measurements it is a good plan to form a table for each magnification used, in which the equivalent values of 1–20 and from this in tens up to 100 scale divisions of the ocular micrometer are given.

It must be understood that the above calculations do not apply to all microscopes made by Leitz. The values for each instrument must be determined by the foregoing method.

Digitized by Google

It is impossible to give an account of the magnifications which may be expected with the oculars and objectives generally in use. They vary much with the different makes, and one should see that a list of magnifications for given oculars and objectives is supplied with the microscope.

The following are the magnifications given by a typical Leitz instrument, 170 mm. tube length. If a revolving stage is attached the tube should be pulled out to the mark 152:—

Objective	Ocular			
	i.	iii.	iv.	v.
2	29	46	58	70
4	91	146	182	218
6	240	384	480	576
Oil-immersion, $\frac{1}{12}$ in.	525	840	1,050	1,260

In order to get the best results in using the oil-immersion lens, the tube should be drawn out to the mark 152, as the revolving stage has a depth of 18 mm.

A difference of 10 mm. more or less makes a great difference in the magnification.

Test slides containing diatomaceous remains are provided with the best German microscopes. A good lens should reveal the presence of actual dots in the diagonal pattern that adorns the cuticle of these organisms.

V.—VARIETIES OF BLOOD-CELLS, AND THEIR SIGNIFICANCE.

(Plate XXVII.)

The average total leucocyte count, as performed on a Thoma-Zeiss hæmocytometer, is 7,000 per c.mm. of blood; a rise above 10,000 indicates a *leucocytosis*, a fall below 5,000 a *leucopenia*. In making a differential leucocyte count at least 300 cells should be counted under the $\frac{1}{12}$-in. immersion lens, and by means of a movable stage the preparation should be moved from side to side, so as not to traverse the same field twice. In a "wave" preparation the edge of the thickened portions will be found to contain the majority of the leucocytes; a knowledge of this fact will save considerable search.

The neutrophile polymorphonuclear.—Normal proportion 60–70 per cent., average 67. Increased in liver abscess, pneumonia, relapsing fever, and in any septic process. Size when spherical, 10 μ. In liver abscess the leucocytosis is not usually considerable unless the pus is under pressure.

Iodophilia.—By this term is meant the affinity which these leucocytes show towards iodine, especially when there is a leucocytosis. The glycogen granules stain a deep brown in a fresh preparation with iodine solution (iodine 1 part, pot. iod. 3, aq. dest. 100), and in this condition they show marked granulation when stained with Leishman.

Lymphocyte.—Normal proportion 19–30 per cent., average 23. The small lymphocyte is 5–8 μ in diameter, the large lymphocyte 8–10 μ. This cell is increased after physiological digestion and in undulant fever, pellagra, and enteric.

Digitized by Google

Large hyaline, or mononuclear (including so-called transitionals).—Size 14–21 μ. Normal proportion 3–8 per cent., average 6 per cent. Increased in all protozoal diseases, malaria, trypanosomiasis, leishmaniasis, and possibly amœbic dysentery. *Nothing under 12 per cent. should be considered a mononuclear rise.* It is now known that the large mononuclears are derived from the myelocyte group and are not related to the lymphoid cells, therefore the so-called transitional cells must be regarded as mononuclears. These cells, as well as the granular polymorph leucocytes, give the *oxydase reaction*—that is, a blue colour with alpha-naphthol and dimethyl-paraphenylene diamine—in the presence of an oxidizing ferment.

Eosinophile.—These cells are a little larger than the polymorphonuclear leucocyte—12–14 μ. Normal proportion 2–4 per cent., average 3 per cent. They are increased in all helminthic diseases—in ascaris, ankylostome, dracunculus, and clonorchis infestations, 5–10 per cent.; in filariasis and paragonimiasis, 10–20 per cent.; and in schistosomiasis and trichinosis, 20–60 per cent. of the total leucocyte count.

Basophile.—Slightly smaller than the polymorph—9 μ in diameter. Usual proportion, 0·5 per cent. The Editor ehas found thm increased in chronic malaria and after long tropical residence, particularly in Central Africa.

Normal red cell (erythrocyte).—Size 7·2–7·5 μ in diameter. Normal number, 5,000,000 per c.mm. Biconcave discs, and therefore considerably thinner in the centre than at the periphery—a feature which must be borne in mind when studying stained specimens. A total red count computed from 64 squares on the Thoma-Zeiss hæmocytometer of under 3,000,000 denotes a severe anæmia and should be accompanied by degenerative changes in the red cells. E.g. malaria, blackwater fever, sprue, ankylostomiasis, Oroya fever.

Nucleated red, normoblast or erythroblast.—Present in very small numbers in normal blood, increased in severe plastic anæmias (e.g. malarial cachexia, blackwater fever, sprue, ankylostomiasis, kala-azar, and Oroya fever), and in severe helminthiasis (*Dibothriocephalus latus*). The nucleus is sometimes double or bilobed, and the protoplasm of the cell is usually polychromatophilic. These cells are generally present in considerable numbers in spleen punctures in kala-azar, severe malaria, Egyptian splenomegaly, pernicious anæmia, and Banti's disease.

Polychromatic degeneration of red cells (Maurer's dots).—Present in subtertian malaria, blackwater fever, and severe anæmias. The term *polychromasia* denotes a degeneration of the red cell, the cytoplasm of which stains light blue; when severe it is generally accompanied by the formation of polychromatic, or basophilic, dots. It is indicative of some toxic absorption, and not pathognomonic of any special disease, for it is found in malaria, verruga Peruviana, pernicious anæmia, ankylostomiasis, and lead-poisoning.

Megaloblast.—Size, two to four times that of a red corpuscle. It is an abnormal nucleated red cell found in severe anæmias, including dibothriocephalus infestations. Their presence in the blood generally indicates a regeneration from the blood-forming cells in the bone-marrow.

Megalocyte.—A red cell of abnormal size and shape, generally associated with microcytes—i.e. small red cells ¼–½ the size of the normal. They are indicative of degenerative changes of the blood in the severe anæmias of blackwater fever, subtertian malaria, Oroya fever, and pernicious anæmia.

Blood-platelets.—These are of no pathological importance. Size about

Digitized by Google

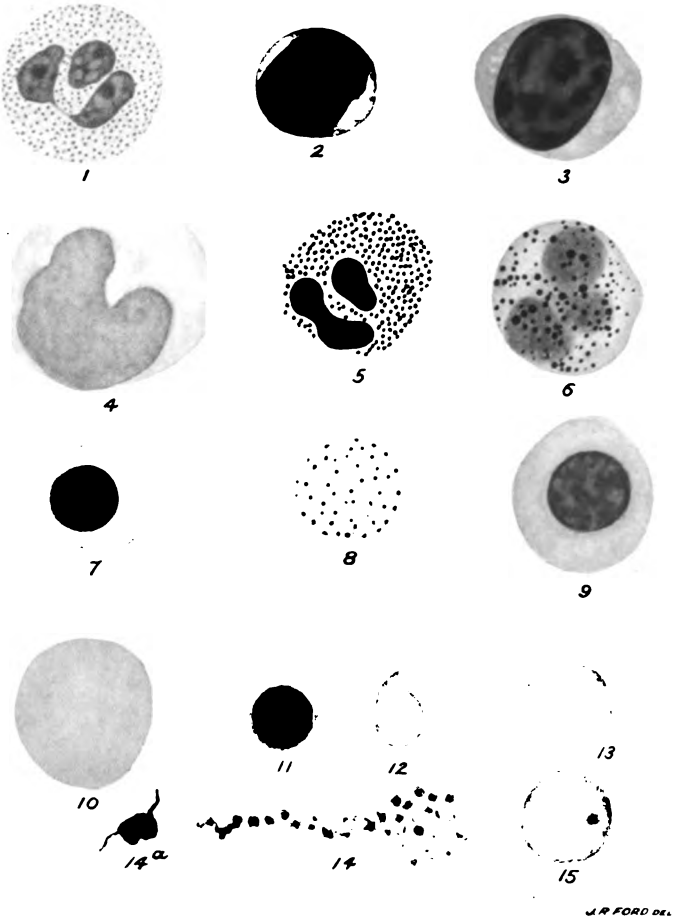
Plate XXVII.

NORMAL AND ABNORMAL BLOOD-CELLS.

1.—Neutrophile polymorphonuclear leucocyte.
2.—Small lymphocyte.
3.—Large lymphocyte.
4.—Hyaline or large mononuclear leucocyte.
5.—Eosinophile leucocyte.
6.—Basophile leucocyte ("mast-cell").
7.—Normoblast (nucleated red cell).
8.—Basophilic dots in red cell (Maurer's dots).
9.—Megaloblast.
10.—Megalocyte.
11.—Microblast.
12.—Microcyte showing poikilocytosis.
13.—Polychromatophilic degeneration of red cell.
14, 14*a*.—Various appearances of blood-platelets.
15.—Blood-platelet superimposed upon a red cell.

Digitized by Google

Digitized by Google



NORMAL AND ABNORMAL BLOOD-CELLS.
× 2,000 diam. (*Leishman's stain.*)

PLATE XXVII.

Digitized by Google

Digitized by Google

3μ in diameter, round, oval, or rod-shaped, according to the viewpoint. When resting on red cells they may simulate malaria parasites, but there is always a clear zone surrounding the platelet. (Plate XXVII., Fig. 15.) When drawn out in making the film they may simulate a trypanosome. They are generally found in masses or in strings, are coated with some adhesive substance and cling to any stationary object. Their function is connected with the clotting of the blood.

VI.—ENUMERATION OF BLOOD-CELLS AND ESTIMATION OF HÆMOGLOBIN

1. Enumeration of Red Blood-Corpuscles by the Thoma-Zeiss Hæmocytometer

This instrument consists of a graduated mixing pipette and a counting slide. The blood is obtained by pricking the finger. It is advisable to give a sharp stab in order to make such a wound that the blood flows freely, so that no squeezing is necessary. The blood is then sucked up to the 0·5 mark on the graduated red pipette, every care being taken not to pass this point. The excess of blood at the end of the pipette should be removed by wiping with a clean cloth. Without delay the blood should be diluted as far as the 101 mark on the pipette with Toisson's fluid, composed as follows:—

Methyl-violet 5 B	0·025 grm.
Sod. chlor.	1·000 ,,
Sod. sulph.	8·000 ,,
Neut. glycerin	30·000 ,,
Aq. dest.	160·000 ,,

Filter before use.*

The pipette should then be taken between the thumb and forefinger and shaken vigorously for one minute so that the blood and diluting fluid become well intermingled. The blood is now in a dilution of 1 : 200. The small amount of fluid remaining in the capillary tube is blown out, while the remainder is transferred to a clean watch-glass.

The blood, diluted in this manner, is placed on to the counting slide as follows: The circular platform of the slide is almost covered with a cover-glass and some of the diluted blood in a capillary pipette is run underneath the free margin. In this manner just sufficient fluid is injected in order to obtain the correct depth of 0·1 mm. for counting purposes.

The blood-cells are permitted to settle for about 3 mins., and the preparation is examined under the low power to ascertain their proper distribution, absence of air-bubbles and foreign bodies. At least four sets of 16 small squares each should be counted with the ⅙-in. objective, and the figure obtained, multiplied by 12,500, will speedily give the total number of red blood-corpuscles per 1 c.mm. of fluid blood.

2. Enumeration of White Cells by the Thoma-Zeiss Hæmocytometer

A special pipette of a larger bore is supplied for this purpose and permits of a smaller dilution of the blood. The diluting fluid is a 1-per-cent. solution of glacial acetic acid in distilled water. The blood is sucked up to the 0·5

* As the result of practical experience, sodium citrate (2 per cent.) in normal saline (0·85 per cent.) is found to act quite as well as Toisson's fluid.

Digitized by Google

mark, the fluid to mark 11, resulting in a 1 : 20 dilution. Once the pipette is filled, it should be placed in a horizontal position, as the fluid is very apt to escape. After shaking, the fluid is transferred to the counting slide as already described, and the cells are allowed to settle for 3 mins. The whole of the 16 larger squares should be counted and the figure obtained multiplied by 312, which will give the total number of leucocytes in 1 c.mm. of blood.

3. The Bürker Counting Apparatus

On this slide, which is a modification of the Thoma-Zeiss, there are two counting chambers side by side, covered by a single cover-glass; thus a red- and a white-cell count can be performed simultaneously. The Bürker is graduated on the same principle as the Thoma-Zeiss, except that one large square on the former corresponds to 16 of the smaller ones on the latter. This counting chamber is most useful for rapidly estimating the number of leucocytes in 16 of the large squares (corresponding to 256 of the small ones of the Thoma-Zeiss). In a normal case the total number of leucocytes counted should vary between 20 and 30 per sixteen large squares; anything above the latter figure indicates a leucocytosis.

As a means of counting the red cells this is by no means so satisfactory as the Thoma-Zeiss method. In a normal blood count it will be necessary to count over 90 separate red cells per big square, whereas in the Thoma-Zeiss apparatus they ought to average about 6 per small square.

For counting the number of minute objects, such as blood-platelets, micro-organisms of vaccines, a much thinner slide known as the *Zappert* has been put on the market. It is so constructed that it can be used with the dark-ground illumination. The slide is graduated to the same dimensions as the Thoma-Zeiss—that is, each square is $\frac{1}{400}$ sq. mm. and the depth of the counting chamber is 0·1 mm. A thin cover-slip is used. The emulsion or fluid is introduced by means of a capillary pipette, as already described.

4. Estimation of Hæmoglobin

The method of estimating hæmoglobin by means of Gower's hæmoglobinometer is the one to be recommended for general use in the tropics. A few drops of distilled water should be placed in the graduated tube supplied with the instrument. A small quantity of blood is drawn up to the graduation mark on the special pipette, and any excess is wiped away from the end. The blood is now transferred to the distilled water in the graduated tube, and by mixing and adding water drop by drop the tint is made to match that of the standard colour tube. The level at which the mixture stands in the graduated tube is now read off. If this be at (say) 60, then the blood contains 60 per cent. of hæmoglobin.

The more rapid blotting-paper test of Tallequist is hardly accurate enough for scientific purposes, though useful as a rough guide.

VII.—PREPARATION OF USEFUL CULTURE MEDIA

Culture media containing solutions of the various sugars should be sterilized by steaming for half an hour on three successive days, and *not by autoclaving*. Prolonged heating under pressure, in the presence of weak acids or alkalis, causes hydrolysis of these substances.

It is advisable, in making media containing *agar*, to prepare batches of two litres rather than smaller quantities, as the unwieldy precipitates obtained

Digitized by Google

in these solutions settle better and are more easily manipulated in large than in small volumes.

In filtering agar media, first allow the precipitate to settle, and decant off the comparatively clear supernatant fluid as far as possible from the flask into the filter. On no account allow the precipitate to come into contact with the filter until the end of the process, otherwise filtration is a very slow and tedious affair.

It is well to sterilize in the autoclave test-tubes which are destined to contain culture media of a composition that cannot be subjected to steam pressure—e.g. sugar media. This procedure ensures complete freedom from spore-bearing organisms such as *B. subtilis*, which is sometimes present in cotton-wool and which cannot be killed by "steaming" alone.

In using the autoclave, great care must be taken to expel all the air from the chamber by allowing steam to issue for a few minutes before screwing down the valve. Otherwise, a mixture of air and steam being present, the pressure indicated on the gauge cannot be accepted as an accurate index of the temperature within.

To boil at 115° C., water requires a pressure of 23 lb. per sq. in.—that is, 8 lb. above the ordinary atmospheric pressure. To boil at 120° C., a pressure of 30 lb.—two atmospheres—is required, and is the amount of pressure usually employed.

After the sterilization process is complete, the autoclave should be allowed to cool down before opening the valve, otherwise there is a sudden development of steam when the pressure is removed, and fluid media will be forced out of the flasks or tubes.

Always add enough water to the autoclave to ensure a residuum when the steam is fully up.

When the Koch sterilizer is employed, it is advisable to put the media into the apparatus while cold. By doing so one can be sure that the whole mass of medium reaches the temperature of 100° C. The period of exposure is reckoned from the time the water in the apparatus begins to boil. In any case, allowance must always be made for the length of time required to raise the temperature of the medium to that of the surrounding steam.

Standardization of media.—1. The most practical method of standardizing the reaction of media for tropical use is the one recommended by Prof. C. J. Martin. The indicator used is α-naphthol-phthalein, 0·05 per cent. in 40 per cent. alcohol. The reaction is adjusted by adding the necessary amount of normal caustic soda, which is estimated by taking out a drop of the medium on the end of a glass rod and placing it on a white tile, previously greased with vaseline, together with an equal amount of the indicator. A hydrogen-ion concentration of 7·6–7·8, or the optimum reaction, will give a *faint olive-green tint*; if too alkaline, a bright green; if too acid, a brownish yellow.

2. *By titration.*—According to Eyre's method, the reaction of a medium may be expressed by the sign + or −, indicating acidity or alkalinity respectively. The degree of either should be expressed by a numerical coefficient indicating the number of cubic centimetres of normal alkali or acid solution necessary to render a litre of the medium neutral to *phenol-phthalein*. The optimum reaction is from + 10 to + 15; to obtain this it is necessary to add 10–15 c.c. of *normal* hydrochloric acid to the litre previously rendered neutral to phenol-phthalein.

Method of titration.—Dissolve all the constituents of the medium and

Digitized by Google

filter; steam for about 40 mins. so as to develop maximum acidity. Add 25 c.c. of warm medium to 25 c.c. distilled water in a porcelain dish containing 1 c.c. phenol-phthalein as an indicator. Titrate with $\frac{N}{10}$ NaOH while keeping the solution hot. It is advisable to make three or four titrations and take the mean. The number of cubic centimetres of $\frac{N}{10}$ NaOH divided by 10 will give the amount of normal NaOH required to neutralize 25 c.c. of the medium. This figure, multiplied by 40, will be the amount of normal NaOH required to neutralize one litre. *The amount of normal soda required to neutralize* 1,000 *c.c. of the medium, less* 10 *c.c., will be the amount necessary to give a* + 10 *or optimum reaction.*

In making final calculations for the addition of normal soda, it must be remembered that the total amount of medium to be standardized will be less by the quantities already used for titration.

Meat extract.—*Composition:*

Minced lean meat	1 lb.
Water	1,000 c.c.

The meat should be placed in a pan together with the requisite amount of water. Simmer the contents gently for 2–3 hours, finally boiling briskly for about 15 mins. The resulting solution should then be cooled and the fat skimmed off the surface with the aid of a piece of wire gauze. When quite free from fat, strain the solution and express as much fluid as possible from the meat that remains by squeezing it through lint.* As this filtration only removes the coarser suspended matter the solution should be filtered finally through paper, the filtrate made up to the original volume and sterilized by autoclaving for 15 mins. at 120° C.

Where it is impossible to obtain fresh beef a substitute may be prepared from Lemco 5 grm., water 1,000 c.c.

Nutrient broth.—*Composition:*

Meat extract	1,000 c.c.
Sodium chloride	5 grm.
Peptone	0 „

Place the meat extract in a flask and add the sodium chloride. In adding the peptone the solution should be agitated to avoid formation of lumps. Steam for about 30 mins. until the ingredients are dissolved, then adjust the reaction. When the solution is quite cold, filter through filter-paper and distribute in tubes. Sterilize by autoclaving 15 mins. at 120° C.

Nutrient agar.—*Composition:*

Meat extract	1,000 c.c.
Sodium chloride	5 grm.
Peptone	10 „
Agar	30 „ (in tropics)

The salt, peptone, and agar should be mixed well together, then added to the *cold* meat extract in a flask. It is advisable to add the ingredients slowly, and to shake well to avoid the formation of lumps. Steam until the ingredients are dissolved, then adjust the reaction. The medium should now

* Boric lint must not be used.

Digitized by Google

be autoclaved for 15 mins. at 120° C., a process which obviates the use of egg-albumen for clearing. After autoclaving, it will be found that a granular precipitate has formed, which easily settles. Filter through lint or cotton-wool; a hot-water funnel is unnecessary. Distribute in tubes, and sterilize in the autoclave for 15 mins. at 120° C., or by steaming for half an hour on each of three successive days.

Glycerin agar is prepared by adding 6–8 per cent. of glycerin to the above, *glucose agar* by adding 1–2 per cent. glucose in the same manner.

Peptone water.—*Composition:*

Sodium chloride	0·5 per cent.
Peptone	1 „ „

Add the sodium chloride and peptone to the requisite quantity of water. Heat for 30 mins. until the ingredients are dissolved. The reaction should then be adjusted. Allow the solution to cool, then filter through filter paper and distribute in tubes. Sterilize by autoclaving for 15 mins. at 120° C.

For growth of the cholera vibrio the solution should be rendered more alkaline.

In case there is any difficulty in obtaining suitable peptone, a medium made as follows is an excellent substitute:

Cole and Onslow's trypsinized casein.—Dissolve 100 grm. of casein in 1 litre of hot 1-per-cent. anhydrous sodium carbonate in tap-water. Cool to 40° C., and add 25 c.c. of pure pancreatic extract and 5 c.c. of chloroform. Digest for 5 days, then add a further 25 c.c. of pancreatic extract and digest for 10 days more. Cool for a day or so to crystallize the tyrosin, and filter. Add 200 c.c. of $\frac{N}{1}$HCl, steam for 30 mins., filter, adjust reaction by the α-naphthol-phthalein method, and finally sterilize. For use in broth, dilute 1 in 3; in peptone water, 1 in 6.

MacConkey's bile-salt and lactose agar, for culture of intestinal organisms.—*Composition:*

Water	1,000 c.c.
Sodium taurocholate	5 grm.
Peptone (glucose-free)	20 „
Agar	30 „ (in tropics)
Lactose	10 „
Neutral red, 1-per-cent. aqueous solution	2·5 c.c.

Mix the taurocholate, peptone, and agar well together, and add gradually to the cold water in the flask; the solution should be agitated to avoid formation of lumps. Steam until the ingredients are dissolved, then adjust the reaction. The solution should now be autoclaved at 120° C. for 15 mins., and the precipitate which forms allowed to settle. Filter through lint or cotton-wool (a hot-water funnel is unnecessary). To the filtrate add the lactose in solution, followed by the neutral red. Distribute in tubes, which should be sterilized by steaming for 30 mins. on three successive days.

Sugar media, for differentiation of the intestinal bacilli.—These media are prepared by adding the various sugars to peptone water (*see* above) containing 0·25 c.c. per cent. of a 1-per-cent. aqueous solution of neutral red, or coloured blue with litmus. In the case of glucose, lactose, saccharose, and mannite, 1 per cent. is added, and in the case of dulcite and maltose, 0·5 per cent. The solution is then distributed in tubes containing Durham's fermentation tubes, and sterilized by steaming for half an hour on three

Digitized by Google

successive days. In tubing off these media, care must be taken thoroughly to wash out the funnel and measure between each batch.

Thomson's serum agar, for cultivation of the gonococcus and other delicate organisms.—This consists of nutrient agar (2·5 per cent. agar) prepared in the ordinary manner from meat juice with 1 per cent. Witte's peptone. The reaction should be set at + 6 Eyre's scale. In place of sodium chloride, the salts of Ringer's solution are used, viz. :—

Sodium chloride	9 grm. per litre
Calcium chloride	0·25 ,, ,, ,,
Potassium chloride	0·42 ,, ,, ,,

Glucose is also added in the proportion of 2·5 per cent. The medium should then be tubed, 4 c.c. to each tube, and sterilized by steaming for half an hour on three successive days. When required, the agar is melted, cooled down to 50° C., and to each tube is added 1 c.c. of human plasma delivered from a sterile pipette. The mixture is then allowed to solidify in a sloping position.

This medium can be used for plate cultures, the agar being melted and cooled to 45° C.; plasma is then added, and the mixture poured into Petri dishes.

Löffler's blood serum, for growth of the diphtheria bacillus.—*Composition :*

Ox-blood serum*	3 parts
1-per-cent. neutral glucose bouillon . . .	1 part

A sufficient quantity of the medium to make a "slant" is placed in a series of test-tubes. The tubes should then be placed in a sloping position and thoroughly inspissated at 65° C. In case an inspissator is not available, good results may be obtained by placing the tubes in a sloping position inside a tin box, and taking care that the medium does not come into contact with the cotton-wool plug. The box should then be put into a Koch's sterilizer, and the temperature gradually raised from the cold to about 65° C., at which temperature it should remain until the serum is thoroughly coagulated. Sufficient normal saline to cover the serum should be added to each tube, and the medium may then be sterilized for 15 mins. at 115° C. When required for use, the saline is poured out of the tube and the medium inoculated in the ordinary way. The advantages of this method are that absolute sterility is easily obtained, and the medium does not dry up on storing.

Trypsin agar.—A most useful medium for growth of *M. melitensis*, the meningococcus and delicate organisms, and for culturing the enteric group for preparation of vaccines or for emulsions for agglutination.

1. *Pea-flour extract.—Composition :*

Pea-flour	50 grm.
Water	1,000 c.c.
Sodium chloride	100 grm.

Add pea-flour and salt to water, mix well and steam for half an hour. Allow to settle, filter, and sterilize.

2. *To make trypsinized broth.*—Remove the fat and the large vessels from bullock's heart, mince the meat finely, and to each half-kilo add 1 litre of

* Camel's serum has been used with good results, but sheep's serum is unsuitable, as it does not set firm enough to form a suitable medium.

Digitized by Google

water. Make faintly alkaline to litmus, and heat the solution to 75°–80° C. for 5 mins. Cool to 37° C. and add 1-per-cent. liq. trypsinæ co. (Allen & Hanburys'); keep at this temperature for 2½–3 hours. When trypsinization is finished, test for peptone by the biuret reaction. Make slightly acid with glacial acetic acid and bring to the boil slowly for 15 mins. Allow to stand overnight. Filter, and make filtrate slightly alkaline to litmus. Sterilize by autoclaving for 1 hour at 118° C. on two successive days.

To make trypagar from trypsinized broth.—To a measured quantity of the broth add 2 per cent. of agar and 0·0215 per cent. of calcium chloride. Autoclave for half an hour at 118° to dissolve constituents. Titrate with $\frac{N}{10}$ caustic soda whilst boiling, and add the necessary amount of alkali to give a neutral reaction. Cool to 60° C., add white of egg (2 to 1,000 c.c.), and steam for two hours. Filter, and to filtrate add 5 per cent. pea extract. Sterilize finally in the autoclave.

For use, sterile rabbit's blood, 5 c.c. to 200 c.c. of agar, is added to the medium at 50° C., or the surface of the medium may be smeared with serum after it has solidified.

Biuret reaction for testing for the presence of peptone in trypsinized media.—Mix 1 c.c. of a 5-per-cent. copper sulphate solution with 5 c.c. of the broth; add 5 c.c. normal caustic soda solution. A pink coloration indicates that trypsinization is sufficient. A bluish-purple colour shows that the process is incomplete.

Bile-salt medium for blood-cultures.—*Composition:*

Water	1,000 c.c.
Sodium taurocholate	20 grm.

Add the sodium taurocholate to cold water contained in a flask, shake well to avoid formation of lumps, steam for half an hour to dissolve, cool, filter, and sterilize by autoclaving at 120° C. for 15 mins. It is convenient to distribute this medium in small flasks, each containing 25 c.c., for the purposes of blood-culture. Whenever procurable, pure ox-bile is preferable to sodium taurocholate medium for blood-culture work. For this purpose it is necessary to visit the slaughter-house and to collect, with moderately aseptic precautions, the bile from the gall-bladder into a flask. The bile is rendered sterile by mixing it well with chloroform (1 oz. to the pint). When treated thus it will keep indefinitely. Before use the chloroform is driven off by gently heating the flask to 60° C. for half an hour.

Crendiropoulo's medium for growth of the cholera vibrio.—*Formula* A:

Peptone	5 grm.
Water	190 c.c.
Sod. hydrate 10 per cent.	10 „

The peptone and water should first be well shaken to avoid formation of lumps, then the sodium hydrate solution should be added. Boil until the peptone is in solution, cool and filter. Sterilize by autoclaving at 120° C. for 15 mins.

Formula B:

Agar	20 grm.
Peptone	5 „
NaCl	2·5 „
Water	500 c.c.

Digitized by Google

Prepare as in the case of ordinary agar. For use, add A to B in the proportion of 2 to 3. It is convenient to tube the solutions in these proportions, so that a tube of agar may be melted, the peptone solution added, and, after thorough mixing, the resulting medium poured into a Petri dish.

Dieudonné's blood-alkali-agar for growth of the cholera vibrio.—*Composition :*

A, equal parts of defibrinated ox-blood and normal caustic soda.
B, ordinary peptone agar.

Add 3 parts of A to 7 parts of B.

It is necessary to allow plates poured with this medium to stand some time before they are inoculated, otherwise no growth occurs.

Nicolle, Novy, and MacNeal medium (N.N.N.), for cultivation of Leishmania and other protozoa.—*Composition :*

Agar	14 grm.
Sodium chloride	6 ,,
Water	900 c.c.

The agar and sodium chloride are added to the water in a flask, well shaken, and dissolved by steaming for two hours. The hot solution is then filtered through cotton-wool, and about 3 c.c. are distributed into each of 50 test-tubes and sterilized in the autoclave at 120° C. for 20 mins. Two large syringes of 25 c.c. capacity are wrapped in a towel and autoclaved with the agar.

Two 100-c.c. Ehrlenmeyer flasks, each containing about 20 glass beads, are sterilized in the hot oven, together with several capfllary pipettes of 5 c.c. capacity. A large healthy rabbit is chloroformed. Immediately after death the heart is exposed with aseptic precautions, and one of the syringes is instantly plunged into it. The blood is then run from the syringe into one of the flasks, and violently shaken until the fibrin is adherent to the beads. Meanwhile the other syringe is used in a similar manner for the second flask. The sterile agar tubes are then liquefied and kept at 37° C. When the blood is defibrinated, about 2 c.c. are withdrawn and added to each tube of agar, which is then rotated to mix the blood and agar. The tubes are then "sloped" upon a glass rod. When the agar has set, the tubes are incubated for 24 hours to test for sterility and to allow them to "sweat." They are now capped or sealed with paraffin wax. Inoculation is effected by introducing suspected material into the "water of condensation"; the tubes are kept at 22° C. and examined 5–7 days later for developmental forms.

Medium for the cultivation of spirochætes.—The culture medium devised by Noguchi for the cultivation of spirochætes consists of—

2-per-cent. agar	2 parts
Ascitic or hydrocele fluid	1 part

A small portion of sterile rabbit's kidney having been added, the whole is covered with a layer of paraffin oil. The medium is inoculated beneath the surface of the oil. Strict anaerobic conditions are necessary. Growth takes place after a period of 10 days at 37° C., or at lower temperatures, as a diffuse haze in the surrounding medium.

In the case of *L. icteroides* and *L. icterohæmorrhagiæ* a mixture of Ringer's solution and one-third rabbit's serum rendered alkaline is covered with a thin layer of sterile paraffin and the material inoculated beneath the surface. The tubes are incubated at 26° C., and growth takes place after 10 days.

Digitized by Google

VIII.—CULTIVATION OF PROTOZOA AND BACTERIA FROM THE BLOOD, CEREBRO-SPINAL FLUID, ETC.

Technique of culture of protozoa from splenic, hepatic puncture, etc.—In making a splenic or hepatic puncture a "Record" syringe (2 c.c.) previously dried with alcohol and ether, and fitted with a fairly large-bore platinum needle, should be used. It is well to start with the plunger halfway down the barrel, so as to provide sufficient air force to expel the contents out of the needle after aspiration. The portion of the spleen jutting beneath the costal margin should be selected, and puncture should be made in two stages, first through the skin, second into the substance of the spleen itself. Traction should be made upon the plunger till blood is seen in the barrel, the object being to remove as much pulp as is possible. In hepatic puncture, the space between the 7th and 8th ribs, in the mid-axillary line, should be selected. The contents of the barrel should be introduced into the water of condensation of N.N.N. medium, and the tubes should be incubated for at least ten days at 22° C. before being examined.

Lymphatic-gland puncture is practised in trypanosomiasis and leishmaniasis. The large gland is held between two fingers, the skin sterilized, and the needle of the syringe inserted; and at the same time the neighbourhood of the gland is massaged. The fluid so obtained may be either cultured or made into films.

Technique of blood-culture for enteric and allied organisms.—To *obtain blood from the vein*, a rubber bandage, or a piece of rubber tubing, should be wound somewhat firmly round the upper arm so as to constrict the brachial vein, thus making the median basilic and cephalic prominent at the bend of the elbow. After painting the skin with a strong solution of iodine, a 10-c.c. syringe should be inserted *upwards* into the most prominent vein and traction gently made upon the piston. Directly the blood begins to flow, the rubber bandage should be loosened or removed. The blood should be allowed to flow up to the 5 c.c. mark. The needle should be then removed from the vein and detached from the nozzle. The blood should be transferred into 25 c.c. of taurocholate broth or bile. The addition of sterile trypsin in the proportion of 1 part to 20 of broth has recently been found to give still more satisfactory results; it inhibits clotting and destroys the anti-bacterial properties of the blood. Should no syringe be at hand, a sufficient amount of blood may be obtained by insertion of a sterilized needle, with rubber tubing attached, into the vein, the blood being allowed to run direct into the medium. This latter method is also applicable to the collection of blood for the agglutination tests and for the Wassermann reaction.

If no other means of obtaining blood is possible, the clot of blood in a Widal tube filled from the finger with aseptic precautions may be utilized after the serum has been abstracted for agglutination reaction.

For more delicately growing organisms such as the meningococcus, *Micrococcus melitensis*, and the pneumococcus, it is advisable to use a larger quantity of medium—50 c.c. of broth in a Florence flask containing no inhibitory constituents.

The test-tubes or flasks should be incubated for 24 hours, and a small quantity of the supernatant fluid removed by means of a sterile pipette or platinum loop and plated out on a suitable medium—i.e. MacConkey's

Digitized by Google

agar for the enterica and allied groups, and trypagar for the more delicate organisms.

The organisms must then be recognized by their biochemical and agglutination reactions. If a negative result is obtained, it is often advisable to leave the blood-culture in the incubator for 48 hours.

Examination of the cerebro-spinal fluid.—*Lumbar puncture* has been little practised in the tropics. Long stout needles as supplied with Barker's syringe must be used, and the space between the third and fourth lumbar spines, on a level with the crest of the ilium, selected. The needle must be inserted boldly in a transverse and rather upward direction.

Normally only about 10 c.c. of fluid are obtained on lumbar puncture, and the pressure rarely exceeds 150 mm. of water. An increase of pressure resulting in a clinical condition known as meningismus is met with in apical pneumonia, scarlet fever, measles, uræmia, eclampsia and epilepsy, typhus fever, cerebral malaria, and sunstroke. Lumbar puncture, by reducing the pressure, greatly relieves the cerebral symptoms.

In *acute infective meningitis*, whether due to the meningococcus or to pyogenic organisms, 20–130 c.c. of cerebro-spinal fluid are obtained by lumbar puncture, and the pressure varies from 200 to 1,000 mm. of water. The fluid itself is turbid and opaque, containing an excessive amount of proteins. The power of reducing Fehling's solution is lost. A cloud of albumen is present. On microscopical examination there is a preponderance of polymorphonuclears, and occasionally large endothelial cells may also be present. Culture on suitable media may reveal the meningococcus, pneumococcus, streptococcus, *B. influenzæ*, more rarely the staphylococcus or *B. typhosus*.

The cerebro-spinal fluid is increased both in pressure and in amount in *meningitis of tubercular origin*. On standing, a cobweb of fibrin may be deposited. The protein increase is mainly due to globulins, and the cell increase to small lymphocytes. Fehling's solution is not reduced. Occasionally, by adding an equal quantity of absolute alcohol and centrifuging, tubercle bacilli may be demonstrated in the sediment. Should this not succeed, the deposit may be injected into guinea-pigs.

The cerebro-spinal fluid shows well-marked changes in 70 per cent. of cases of *secondary syphilis*. There is an exudation of lymphocytes, an excess of globulin, and a positive Wassermann reaction. In both interstitial and parenchymatous tertiary syphilis the fluid is increased in quantity and pressure, and contains an excess of lymphocytes. In tabes and general paralysis the fluid gives a positive Wassermann reaction, according to Craig, in 80–90 per cent. of cases. A similar result is obtained with the serum alone in 70–80 per cent.

In the late stages of *sleeping sickness* trypanosomes can be demonstrated in smears obtained from the centrifugalized deposit of cerebro-spinal fluid. Pleocytosis—an excess of small and large mononuclears—is noted in the cellular exudate. In doubtful cases inoculation of the fluid into dogs or monkeys yields definite results in 10–14 days. This procedure constitutes a test of great clinical importance.

The Nonne-Apelt test for globulin in the cerebro-spinal fluid.—Add equal quantities of the fluid to a saturated solution of ammonium sulphate. An opalescent ring forms at the junction with the fluid, and, on shaking, a general opalescence ensues in 3 mins. if globulin is present.

Digitized by Google

IX.—AGGLUTINATION WITH PATIENT'S SERUM FOR TYPHOID, PARATYPHOID, AND WEIL-FELIX REACTION

The microscopic method of performing the Widal reaction is by no means so reliable as the various macroscopic methods, the results of which are much more obvious, and which, moreover, permit the end-point of agglutination to be determined with greater accuracy.

A simple method of macroscopic agglutination by progressive dilution of the serum in agglutination tubes can be employed, but gives only a limited range of dilution, and a considerable amount of blood (1–2 c.c.) is required. The glass capsules containing the blood should be centrifuged, and the serum abstracted by means of a pipette. At least 5 drops of clear serum are required in order to obtain a quantity sufficient for further dilution. This amount should be mixed with 20 drops of normal saline delivered from the same pipette held vertically, in order to obtain a 1 : 5 dilution. For further dilution 20 drops of the 1 : 5 dilution are placed in the first of a row of agglutination tubes, after which 10 drops are removed and mingled with an equal amount of saline in the second tube, thus giving a dilution of 1 : 10. From these 20 drops 10 are removed and placed in a third tube, and so on, the dilution each time being doubled. To the 10 drops of diluted serum remaining in each tube an equal amount of an opalescent bacillary emulsion should be added, thus doubling the dilution of the suspension in which the organisms are placed. The tubes are incubated for 2½ hours or, preferably, for a shorter period at 55° C., and are then examined for agglutination against a dark background; this is generally sufficiently obvious when compared with control tubes in which bacillary emulsion diluted with saline or with normal serum has been placed. The objection to this method is the limited range of titre which it affords; in order to get a range of from 1 : 10 to 1 : 160, a row of five tubes is necessary.

In testing for typhoid and paratyphoid agglutinins three rows of five tubes each are necessary—one for typhoid, and one each for paratyphoid A and B.

In describing the various methods the following abbreviations are commonly used, viz.: "T" for typhoid, "A" for paratyphoid A, and "B" for paratyphoid B.

A more practical, but more tedious, method is Dreyer's drop method, for which standardized bacillary emulsions can be obtained. A stand containing 15 agglutination tubes in three rows of five each, and two larger dilution tubes, should be taken. With a dropping pipette measure out into one dilution tube 54 drops of normal saline solution (0·85 per cent. sodium chloride in distilled water) by means of gentle pressure on the teat. Wash the pipette with distilled water, and subsequently with absolute alcohol and ether, so as to dry thoroughly. Take up the serum to be tested into the dried pipette. Measure out 6 drops of the serum into the dilution tube already containing the 54 drops of saline, thus obtaining a dilution of 1 : 10.

The second tube should be taken, and 3 drops of the 1 : 10 serum dilution added to 57 drops of normal saline; this gives a dilution of 1 in 200. The pipette should be carefully washed out, and to each tube in the row 15 drops of standard agglutinable emulsions of T, A, and B added. Thus:—

① ② ③ ④ ⑤	① ② ③ ④ ⑤	① ② ③ ④ ⑤
T	A	B
15 drops	15 drops	15 drops

Digitized by Google

For the addition of the diluted serum it is best to commence with the higher dilutions before proceeding to the lower ones. To tube 3 in each row add 10 drops of 1 : 200 serum ; to tube 4 in each row add 5 drops of 1 : 200 ; to tube 1 add 10 drops of 1 : 10 dilution, and to tube 2 also add 2 drops of 1 : 10 dilution. The pipettes must be washed out before proceeding to the saline. The addition of saline should then be made to tubes 2 and 4, which receive 8 and 5 drops respectively, while tube 5 receives no serum, but 10 drops of saline only, and acts as a control against spontaneous agglutination. This can be best represented by the following scheme :—

No. of tube	*Drops of normal saline*	*Drops of serum*
		Dilution of 1 : 10
1	0	10
2	8	2
		Dilution of 1 : 200
3	0	10
4	5	5
5	10	0

It will be noted that the final volume of fluid in each tube, when the bacillary emulsions are added, is 25 drops. By mathematical calculation it will be seen that in tube 1 of each row the serum acts in a dilution of 1 : 25.

In tube 2 in a dilution of 1 : 125
„ 3 „ „ 1 : 500
„ 4 „ „ 1 : 1,000

This method gives a large range of titre and may be adopted for other pathogenic organisms as well.

The tubes are examined after four hours at 37° C., or two hours at 50°–55° C., followed by 15 minutes' sedimentation at room temperature. The reading is taken by comparing each tube in succession with the control tube, and is preferably made by means of artificial light against a black background. If daylight is used, the tubes should be partly shadowed by passing a finger up and down behind them.

There is evidence to show that the sensitiveness of these emulsions is affected by storage in the tropics. Wherever it is possible, it is advisable to make fresh opalescent emulsions from agar cultures of the organism concerned.

Stands and dropping pipettes can be obtained from Messrs. Baird & Tatlock, and the standard emulsions from the Department of Pathology, Oxford University.

Rapid method of macroscopic agglutination by Garrow's agglutinometer (Fig. 386).—This is a practical method suitable for small laboratories. It may be used for the recognition of pathogenic bacteria isolated from the blood or excreta by means of specially prepared serums. Macroscopic agglutination becomes visible in as short a period as three minutes; no incubator is needed.

For use the following apparatus is required :—

(1) A *painter's palette* (Fig. 387) for dilution of the serum. (2) A *diluting pipette* drawn from glass tubing ¼ in. in diameter and 6 in. in length. The former should deliver a drop of satisfactory dimensions (a Donald's pipette fitting Morse gauge No. 70 is the correct size), and is such that when mingled with an equal quantity of bacterial emulsion it does not run over the edge of the glass slab. (Fig. 388.) (3) The *agglutinometer slab*, a piece of plate glass

Digitized by Google

11½ in. long by 1½ in. wide, divided into a number of partitions by double grooves running at regular intervals of 1 cm. in order to prevent the dilutions from intermingling. (4) *Set of bacterial emulsions.* The stock emulsions for use with the agglutinometer for the diagnosis of enteric are *B. typhosus*, *B. paratyphosus* A, B, and C; for undulant fever, *M. melitensis* and *M. paramelitensis*; for bacillary dysentery, *B. shiga* and *B. Flexner*-Y. They are made from 24-hour surface agar cultures. The growth is scraped (not washed) off the surface by means of a platinum loop and emulsified in 0·2-per-cent. formalin in normal saline. The emulsions should be very dense, of milky consistency and uniform suspension.

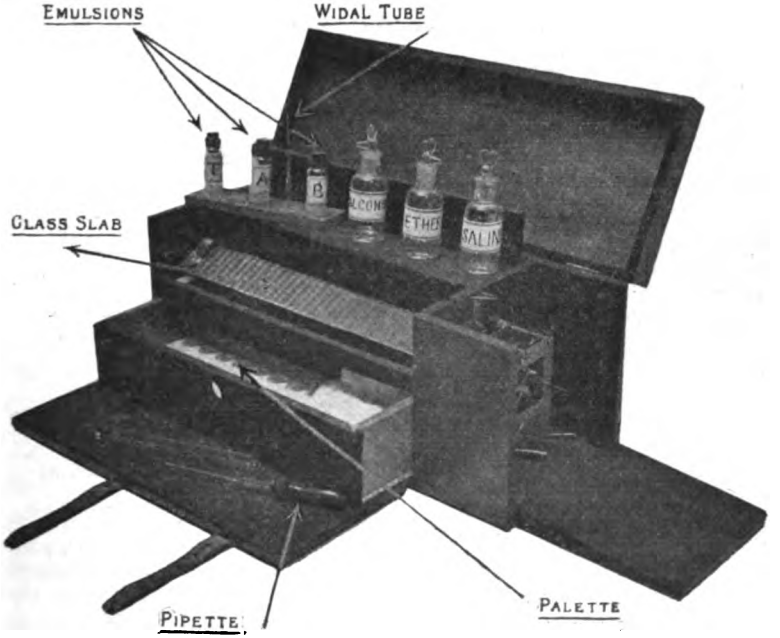


Fig. 386.—Garrow's agglutinometer, for rapid macroscopic agglutination.

In order to promote the intimate mixture of the serum under investigation and the bacillary emulsions, the slab is made to revolve by means of clockwork at a uniform rate of about 15 revolutions per minute. For field use the slab may be placed in a simple box provided with damp blotting-paper in order to obviate desiccation, and turned by hand by an iron handle attached to a wooden shaft which supports the glass slab.

The diluting process.—The blood for examination is taken from the finger and collected in a Wright's capsule. Three large drops of blood are sufficient; the ends of the tube being sealed with wax or plasticine. (Fig. 389.) After standing for some time the serum separates, rendering centrifugalization unnecessary. By means of the pipette 2 drops of clear serum are abstracted and placed in the first partition of the mixing palette. In order to make a

Digitized by Google

dilution of 1 : 5, 8 similar drops of normal saline are added. From the resulting 10 drops of diluted serum, 5 are then placed in the next partition and a similar amount of saline added; and so on, thus making a series of dilutions from 1 : 5 to 1 : 80 or more. It is important that the pipette be held vertically throughout the process, to ensure equality in size of the drops.

The mixing process.—The process of mixing the blood serum and bacterial emulsion is carried out on the agglutinometer slab. It is essential that the slab be perfectly free from grease, or the drops will not run together. It should

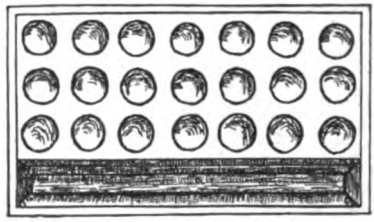


Fig. 387.—Palette for diluting serum.

be cleaned after each test by (1) washing in 1 : 20 carbolic acid, (2) cleaning with alcohol, and (3) drying with ether. It is a good plan to keep a piece of old linen specially for this purpose. In cold weather the drops can be made to run more freely by gently heating the slab before use.

Holding the pipette vertically, begin with the highest dilution, and deposit drops of the various dilutions of serum in triplicate (if, for example, agglu-

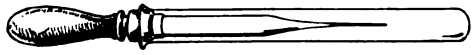


Fig. 388.—Pipette for use with agglutinometer, showing method of protecting the point. One-third nat. size.

tination against T, A, and B is being carried out) on the slide. Opposite each drop of serum place a drop of bacterial emulsion, sterilizing the pipette by drawing into and expressing from it (1) alcohol, (2) ether, between each emulsion.

Fig. 390 shows the appearance of the slab after carrying out the above process.

Fig. 389.—Type of tube for collecting blood. Nat. size.

The slide so prepared is placed in the moist chamber of the mechanical mixer, where it is held fast by means of a clip at each end of the shaft. The clockwork is put into operation and the slide is allowed to revolve slowly for 3 mins. The result is that the drops of diluted serum run into and mix freely with the corresponding equal drops of bacterial emulsion, producing mixtures having serum titres of $\frac{1}{10}$, $\frac{1}{20}$, $\frac{1}{40}$, and so on. (Fig. 391.)

At each complete revolution of the slide the bulk of these mixtures runs to and fro across the slide. At the end of 3 mins. the clockwork

Digitized by Google

is stopped and the slide removed and examined by the naked eye (if necessary, by a pocket lens) in a good light against a dark background. Agglutination converts the mixtures from homogeneous milky emulsions into a condition in which the agglutinated masses of bacilli float about like minute flakes in a clear fluid. In a strongly agglutinating serum this takes place almost instantaneously after the agglutinometer slab begins to revolve. In higher dilutions the change may take 3–4 mins., and be observable only with the aid of a pocket lens. If no change is visible with the pocket lens in the 1 : 10 dilution at the end of 5 mins., no agglutination of any diagnostic significance is present in the blood.

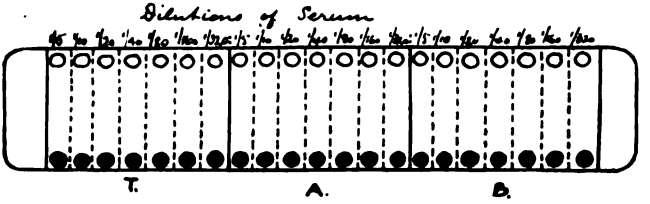


Fig. 390.—Slab with bacillary emulsions and dilutions of serum.

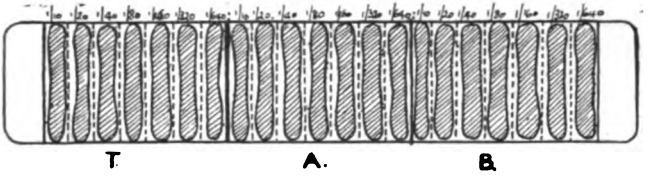


Fig. 391.—Intermingling of serum and bacillary emulsions.

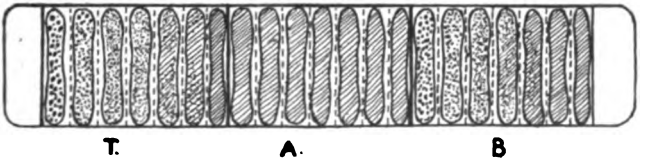


Fig. 392.—Reaction complete : showing appearances of agglutination.

Fig. 392 shows the appearance of the agglutinometer slide in the case of a patient whose blood agglutinates T up to 1 : 320, B up to 1 : 160, the A emulsion being negative.

Significance of agglutination in enteric.—(A) *In uninoculated persons :* A positive agglutination to T, A, or B in 1 : 10 or over during the first week of illness may be considered to be diagnostic.

(B) *In persons inoculated with a single vaccine* (T, for example).—The agglutinins to these respective organisms appear in the blood after inoculation on the fifth day, reaching a maximum titre of 1 : 1,200 on the twelfth, then gradually falling for the next 16 months, when they finally disappear. These are known as *residual agglutinins*. Should a person thus inoculated become infected with typhoid or paratyphoid, a marked fluctuation of these

Digitized by Google

residual agglutinins takes place, indicating that the immunity apparatus is under stimulation. For instance, in a B infection, the T agglutinins will rise before the agglutinins to B make their appearance. Taking all things into consideration, in such a case an agglutination of less than 1 : 320 within six months of inoculation should not be considered diagnostic. In any case, it should be confirmed by repeated tests at three days' intervals in order to observe the rise in titre to one or other of these organisms. In A infections no preliminary stimulation of the T agglutinins takes place, and the agglutinins specific to A may not appear till late in the disease, at any rate until after the tenth day. The agglutinogenic power of A is very feeble, and a titre of 1 : 10 to this organism in a straightforward case should be regarded as diagnostic.

Diagnosis of enteric in T, A, B inoculated persons.—In this case it is necessary, should the clinical symptoms be suspicious, to test the agglutinins on several occasions during the course of the fever to ascertain whether the titres for T, A, or B are remaining constant or rising or falling, always remembering that the residual agglutinin to A is a very low one.

NOTE.—The necessity for an intelligent interpretation of agglutination results, in conjunction with the clinical facts of the case, is paramount. Only the isolation of the responsible organism by hæmoculture renders the diagnosis absolute. The moral is that every aspect of a case of prolonged pyrexia in a previously inoculated subject must be interpreted, and all the facts of the case taken into consideration.

Agglutination in undulant fever.—The agglutinins of *M. melitensis* and *M. paramelitensis* sometimes appear in the blood only in the third or fourth week of the disease. Attention must be paid to a curious phenomenon called the *inversion phenomenon*. For instance, agglutinins may be present in the higher but not in the lower dilutions. In undulant fever cases a dilution of 1 : 10 may be regarded as diagnostic.

Weil-Felix reaction in typhus.—The patient's serum is agglutinated against a suspension of X 19 or *B. proteus*. An agglutination by the macroscopic method of over 1 : 20 on the fifth day of the disease is regarded as diagnostic. A dense emulsion of the organism should be used.

X.—RECOGNITION OF ORGANISMS ISOLATED FROM THE FÆCES AND URINE BY AGGLUTINATION

An emulsion of a pure culture of the organism is made in saline and tested on the agglutinometer, or in tubes, against specific serums such as are supplied by the Lister Institute.* In routine examinations it is convenient to keep the stock dilution of the serum (say 1 : 50) in small rubber-stoppered bottles in 0·5-per-cent. carbol saline. If the organism is agglutinated in a dilution of 1 : 100, it is tested against higher dilutions and the titre thus determined.

For special method of employing agglutination in the diagnosis of cholera, *see* p. 395.

Cultivation of pathogenic organisms from the fæces. (1) *Dysentery.*—If the stool is pure blood and mucus, a loopful is spread in a spiral manner on a MacConkey's agar or litmus lactose-agar plate. If fæces are present, a portion of the blood and mucus is selected and washed in sterile saline

* These are prepared from the serum of rabbits injected with killed emulsions, such as cholera, Shiga, Flexner-Y, T-A-B, *Micrococcus melitensis*, etc.

Digitized by Google

to free it from contamination, then plated as described above. The plates are incubated for 24 hours, and subsequently suspicious colonies are picked off and subcultured on agar. The agar tubes are incubated overnight, and the resulting culture is agglutinated against specific serums as already described.

(2) *Enteric group.*—A small portion of the stool is emulsified in 5 c.c. of saline, and one platinum loopful of the resulting emulsion spread on a MacConkey's agar plate. Great care should be taken not to spread it too thickly, otherwise the resulting colonies will be too dense; it is recommended that the same loop should be inoculated on to three or more plates. The colonies are small, clear, and drop-like, and are recognized in the manner described above.

Cultivation of pathogenic organisms from the urine.—For this purpose a catheter specimen is essential. The urine is allowed to sediment for six hours, at the end of which time about ½ c.c. of the deposit is spread on a 6-in. MacConkey plate. The latter is incubated for 24 hours, and the colonies are recognized by their serological reactions.

Isolation of pathogenic organisms post mortem in enteric, dysentery, cholera, and plague.—In the case of the solid organs (spleen, liver, and kidney) the external surface should be seared with a hot glass rod, then incised with a sterile knife, and the pulp removed with a sterile platinum loop and plated on MacConkey or ordinary agar. In the case of the urinary and the gall-bladder the external surface should be seared as above and a portion of the contents taken up into a sterile syringe, from which the material can be transferred to the culture media.

For the isolation of the dysentery bacillus from the intestine, the reader is referred to p. 420.

In stained films of material obtained post mortem, the only bacillus which can be recognized with anything like certainty is that of plague, owing to its peculiar bipolar staining character, but even in this case it may be simulated very closely by other organisms such as that of malignant œdema, *pseudopestis*, and also by saprophytic organisms.

XI.—CHEMICAL AND MICROSCOPICAL EXAMINATION OF FÆCES

Reaction.—A small portion of the stool should be rubbed up in a mortar with distilled water to a soup-like consistency. A drop of the fluid should then be applied by means of a glass rod to a piece of blue or red litmus paper which has been previously moistened with distilled water. The reaction is easily seen on the reverse side of the test-paper. A normal stool should be nearly neutral; a marked acid reaction indicates fermentation, a marked alkaline reaction putrefaction.

Bile pigment.—Mix a small portion of the stool with a concentrated solution of perchloride of mercury and allow to stand 24 hours. A normal stool turns red owing to the presence of hydrobilirubin, whilst a green colour is indicative of unaltered biliverdin.

Benzidin test for detection of small quantities of blood in the stool.—Emulsify a portion of the fæces about the size of a pea in 5 c.c. of distilled water. Place the emulsion in a test-tube and boil for a minute in order to destroy any enzyme present, then cool. An approximately saturated solution of benzidin is made by dissolving a knife-point of pure

Digitized by Google

benzidin in about 2 c.c. of glacial acetic acid in a *clean* test-tube. Into another clean test-tube pour 10–12 drops of the fresh benzidin solution and from 2½–3 c.c. of hydrogen peroxide (3 per cent. H_2O_2) and shake the tube lightly. No green or blue tints should appear in this mixture of reagents. A few drops of the fæces emulsion are now added, when, in the presence of blood, a beautiful green, bluish-green, or blue coloration will appear. The depth of the colour and the length of time it takes to appear depend upon the amount of blood present. Later the colour changes to violet. Only a green or blue colour can be regarded as positive, and practice soon teaches what degree of colour-change is indicative of occult blood. It should be noted that saliva, pus, mucus, iron salts, and iodides may also give a reaction with benzidin.

Microscopical examination and recognition of various elements in the fæces (Fig. 393.)—*Muscle-fibres*, derived from meat, practically always occur in the stools, and are recognized by their cross-striation. When present in large numbers they indicate defective intestinal digestion.

Connective tissue, derived from meat, resembles mucus somewhat; it is distinguished by striation, which disappears on addition of acetic acid. When present in large masses, defective gastric digestion may be inferred. Elastic fibres have no significance.

Starch granules, derived from fruit and potatoes, are stained blue by addition of iodine solution. They vary in size and shape, according to the food from which they are derived. Well-preserved granules with concentric markings are seldom seen. They are often enclosed in a cellulose covering, but are not liable to give rise to much difficulty, except those derived from peas and beans, which roughly resemble the eggs of tapeworms.

The presence of excess of starch is pathological, and such a stool is usually acid and shows signs of gas-bubbles, fermentation, and presence of yeasts. It is an interesting point that starch is never bile-stained. The iodine test may be applied to ascertain the extent to which the starch has been digested. A blue colour indicates unchanged granules; red, that they have been slightly digested.

Detritus which is derived from fruits and vegetables is easily recognized by its spiral ducts, areolar tissue, vascular bundles, and pigment cells.

Neutral fats, derived from the fat of food, are recognized as colourless, highly refractile droplets, or sometimes as irregular bile-stained masses which are stained by Sudan III. and are soluble in ether.

Fatty acids, derived from the fat of food, occur as sheaves of colourless acicular crystals, which melt on being warmed and dissolve in ether.

Soaps, derived from the fat of food, occur as greasy-looking amorphous masses, or sometimes as needles which are thicker and not so long as those of the fatty acids. They may be colourless, or stained with bile pigments. They are not soluble in ether, as are the fatty acids, and do not melt on being warmed. If the film of fæces on a slide is treated with acetic acid and heated, fatty-acid crystals will be seen to separate out.

Fats may be distinguished from mucus or from vegetable material by the following rough test: Prepare a smear of the stool on a slide, put on a cover-slip, and press the latter down on to the smear: should the material be of fatty composition the cover-slip will remain down; if vegetable detritus or mucus, it will spring back when the pressure is taken off.

In a normal stool, fat is present almost entirely in the form of amorphous masses of soap, less often as crystals. Neutral fat ought to be absent.

Digitized by Google

Mucus occurs as transparent shreds, sometimes bile-stained. It has always a pathological significance, and when containing leucocytes and epithelial cells indicates intestinal ulceration.

Intestinal sand.—The appearance of sand grains in the stools of persons who live where desert conditions exist is extremely frequent, and is due to the ingestion of this substance together with the food. These cases must

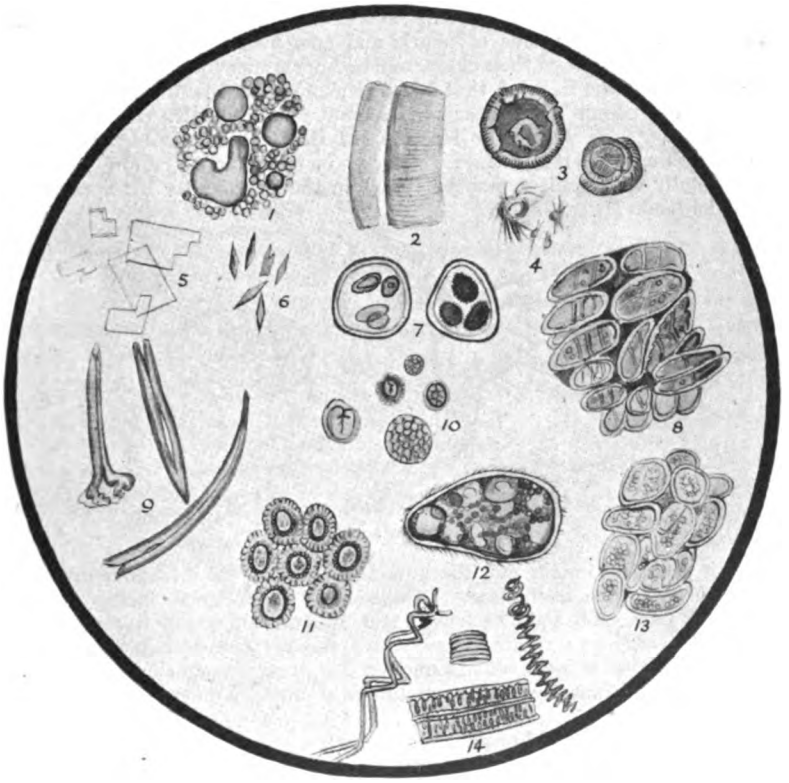


Fig. 393.—Microscopic appea ance of common objects in the fæces. × 800 diam. (*Orig.*)

1, Casein and fat dropl ts; 2, muscle-fibres; 3, soap crystals; 4, crystalline fatty needles; 5, cholesterin crystals; 6, Charcot Leyden crystals; 7, truffle spores; 8, portions of husks of cereals; 9, hairs of wheat grain; 10, spores of fungi; 11, cells from pericarp of peas; 12, parenchyma of beans; 13, endosperm of rice; 14, vegetable spirals.

not be looked upon, therefore, as true instances of the secretory neurosis known as intestinal sand.

Charcot-Leyden crystals are frequently found in stools containing entamœbæ, but are practically always absent from acute bacillary dysentery stools. They may also occur in other intestinal parasitic infections.

Pseudo-parasites.—Of the larger intestinal parasites which can be seen with the naked eye, care must be taken not to mistake, as frequently happens,

Digitized by Google

the pulp of orange for trematodes, banana fibres for small tapeworms, or pieces of cotton-thread and celery for *Oxyuris vermicularis*, *Ankylostoma duodenale*, etc. As regards the microscopic diagnosis, numerous objects may be mistaken for the eggs of parasites, and it is important that the tropical worker should be able to recognize various articles of diet as they appear in the stools. The spores of truffles, which occasionally appear in the fæces, may be mistaken for ova of *Ascaris lumbricoides*, owing to their size (42–66 μ) and rough surface. The spores of mushrooms have a similar appearance. Pollen grains of plants and spores of fungi have given rise to difficulties, in spite of their characteristic appearance under the microscope. It should be borne in mind that the pollen of conifers is often met with in the stools of people living near pine forests. No difficulty will be experienced in diagnosis when it is remembered that all these spores are really globes with a reticulated surface which can be made out on careful focusing. Occasionally cheese-mites may be found in the fæces after being ingested with the food. (Fig. 394.)

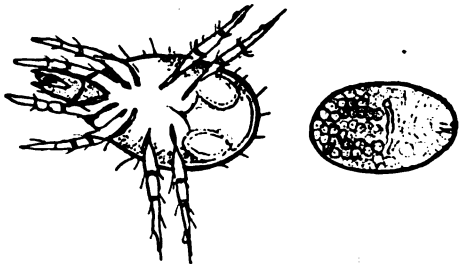


Fig. 394.—Cheese-mite (Tyroglyphus) and egg of same in fæces. × 200 diam. (*Orig.*)

It is difficult to make out the nuclear details of the intestinal protozoa and their cysts in a fresh state. The addition of Weigert's iodine solution (iodine 1 part, pot. iod. 2 parts, water 100 parts), which has a special affinity for nuclear structure, and which renders the details much more evident, constitutes a convenient method for their recognition. For permanent preparations fæcal films should be stained by one of the following methods:—

Schaudinn's method of staining protozoa in fæces.—All the intestinal protozoa are delicate organisms, and must be fixed for staining purposes by wet fixation. The classical method, Schaudinn's, is carried out as follows:

A. *Schaudinn's fluid.*
Absolute alcohol, 50 c.c.
Saturated solution of corrosive sublimate in water, 100 c.c.
Glacial acetic acid, 1–5 c.c.

B. *Heidenhain's hæmatoxylin.*
1 gramme hæmatoxylin dissolved in 10 c.c. boiling alcohol is added to 90 c.c. distilled water, and kept in a strong light for about four days in the tropics, when 100 c.c. more of distilled water are added.

C. 4-*per-cent. iron alum.*
Four grm. of iron alum crystals are dissolved in 100 c.c. of distilled water with the aid of a pestle and mortar.

Digitized by Google

Fairly thin preparations of fæces, preferably with the addition of mucus, are made on clean cover-slips and floated film downwards in solution A, and left to fix for half an hour, when they are reversed.

(1) Wash in several changes of 70-per-cent. alcohol.
(2) Leave in 70-per-cent. alcohol and Lugol's solution (a few drops) for half an hour. Wash in hyposulphite of soda solution (a crystal in 25 c.c. distilled water) to remove iodine, and wash in water.
(3) Place in solution C and leave 12–24 hours.
(4) Wash rapidly in water and leave in solution B for 12 hours.
(5) Again wash in water.
(6) Transfer to 1-per-cent. iron alum.
(7) Decolorize in this solution under the microscope and leave till nuclei are clear.
(8) Transfer to water.
(9) Wash rapidly in 50-per-cent., then 70-per-cent., alcohol.
(10) Pass through absolute alcohol with two changes.
(11) Absolute alcohol and xylol, equal parts; wash in xylol and mount in Canada balsam.

In addition to the iodine method of demonstrating protozoa in fæces the following confirmatory quick-staining methods are recommended by Dobell.

METHOD I

(1) Fix films for 10–20 minutes in Schaudinn's fluid as before.
(2) 70-per-cent. alcohol, two changes.
(3) 70-per-cent. alcohol and iodine 10 mins.
(4) Distilled water after hyposulphite of soda solution.
(5) Hæmalum (Mayer's) 15–20 mins.
(6) Running water till blue.
(7) Through alcohols, alcohol and xylol, xylol.
(8) Mount in Canada balsam.

METHOD II

1-per-cent. hæmatein in 70-per-cent. alcohol = stain.
*1-per-cent. iron alum in 70-per-cent. alcohol = mordant.
(1) Fix films in Schaudinn's fluid as before for 10–20 mins.
(2) Wash in 70-per-cent. alcohol.
(3) 70-per-cent. alcohol and iodine, 10 mins.
(4) Mordant, 10 mins.
(5) Alcohol 70 per cent., several changes.
(6) Stain, 10–20 mins.
(7) Wash in 70-per-cent. alcohol.
(8) Differentiate with mordant under microscope.
(9) 70-per-cent. alcohol, several changes.
(10) Absolute alcohol, two changes.
(11) Absolute alcohol and xylol.
(12) Xylol.
(13) Mount in Canada balsam.

Sections fixed in Zenker's fluid are stained in the same manner, save that they are differentiated in acid alcohol 0·6-per-cent. instead of in iron alum, and are left to blue in running water.

* Dissolve 1 grm. of iron alum in 2 c.c. distilled water, and add 77 c.c. of 96-per-cent. alcohol.

Digitized by Google

XII.—EXAMINATION OF URINE

The methods of urinalysis in the tropics do not differ materially from those employed in general medicine. Owing to the excessive perspiration the total amount of urine passed may be considerably less than in colder climates. The determination of the presence of albumen and of its variations quantitatively from day to day is very important, especially in yellow and blackwater fevers. The presence of indican and the diazo-reaction are useful confirmatory tests in enteric fevers, sprue, etc.

Jaffé's modified method for indican.—To 5·c.c. of urine add an equal quantity of concentrated hydrochloric acid, followed by 2 c.c. of chloroform, and allow to stand for a few minutes, then add 3 drops of a 3-per-cent. potassium chlorate solution. If indican is present the chloroform will be tinged blue.

The diazo reaction.—Two solutions are necessary for this test—(A) a saturated solution of sulphanilic acid in 5-per-cent. hydrochloric acid, (B) a ½-per-cent. solution of sodium nitrite. The solutions should be as fresh as possible. To some urine in a test-tube add an equal quantity of (A), then three drops of (B), and shake till froth forms. Make alkaline with ammonia. A positive reaction is indicated by a port-wine coloration of the solution, while the froth is also red.

Russo's methylene-blue reaction.—Four drops of a 1-per-cent. watery solution of methylene-blue are added to 4 or 5 c.c. of the patient's urine and thoroughly mixed. When held against the light the resulting mixture has an emerald-green colour without a trace of blue. This reaction is more sensitive than the diazo, and appears about the same time in enteric fevers and in infectious jaundice.

Urobilin.—To some unfiltered urine contained in a test-tube add an equal amount of a saturated solution of zinc acetate in absolute alcohol. The tube should be shaken, and a few drops of Lugol's solution added. On filtering the solution, fluorescence in the filtrate shows the presence of urobilin. The degree of blood destruction is indicated by the intensity of the fluorescence. This should be verified by the spectroscope.

This test is useful in those diseases, especially malaria, of which hæmolysis is a feature.

Red blood-corpuscles are seen in cases of urinary schistosomiasis. The urine should be examined as soon as voided, as under certain conditions the red cells become rapidly disintegrated. They may appear with a fairly normal outline, shrunken, or swollen, according to the density of the urine.

Leucocytes and pus-corpuscles occur in any inflammation of, or abscess-formation in, the urinary tract. Their origin is indicated by the other constituents, such as the character of the epithelial cells and the presence of casts. Pus-cells in gonorrhœa may be mixed with mucus threads which settle to the bottom of the glass. In alkaline urine the pus-cells swell and the mass becomes gelatinous. In acid urine the cells may be shrunken and cloudy, and the addition of acetic acid may be necessary to bring out the nucleus. Albumen is always present in small amount in a urine that contains pus.

Organisms present in urine indicate a bacilluria; if present in large clumps and intermingled with renal epithelium, the existence of *B. coli* pyæmic abscesses in one or both kidneys should be suspected (*see* p. 312).

The organisms of the enteric group may also be visible by microscopic examination, and require further investigation for their recognition.

Digitized by Google

Finally, the eggs of *S. hæmatobium* or *S. mansoni* (160 μ by 60 μ) may be present in urine which contains no recognizable blood. The specimen should be allowed to stand or be centrifuged, and the deposit examined under a low power. If schistosomiasis is suspected and no eggs are discovered, the character of the pus-cells in the exudate should be taken into consideration; if mostly eosinophiles, a further search for ova is suggested. A rectangular glass vessel 1½ in. in length by ⅜ in. in depth, as used in eye hospitals, and which can be placed on the microscope stage, is a convenient receptacle for the examination of urinary sediment and for demonstrating the escape of the miracidia from the ova.

Donné's pus test.—The supernatant fluid should be decanted and a strong solution of NaOH added to the sediment; if it be pus, it will be transformed to a gelatinous mass which adheres to the glass.

In chyluria, nucleated granular corpuscles similar to leucocytes, and considerable amounts of very finely divided fatty material, are present in the urine. If the patient comes from a district where filariasis is endemic, the blood and urine should be carefully searched for the presence of microfilariæ.

Epithelium.—It is normal for a few bladder or urethral epithelial cells to be present in the urine. The number of these cells is increased in inflammatory and destructive lesions, and, when this is the case, cells from the lower layers of the urinary tract, normally never present, may appear. In addition to these the following varieties may be recognized:

1. *Renal epithelium.*—This is round, polygonal, or cubical in shape, and nucleated. In size the cells may be a little larger than leucocytes (22–25 μ). The protoplasm may show fatty degeneration or be disintegrated. They are liable to become distorted and swollen by the action of the urine so as to bear a rough resemblance to *Entamœba histolytica*, for which they should on no account be mistaken.

2. *Casts.*—These are divided into three main classes, the cellular, granular, and amorphous. The last of these have a homogeneous structure and occasionally show a faint striation.

Cellular casts.—The cells composing these cysts may be formed either of renal epithelium, leucocytes, or red blood-corpuscles. These elements can easily be recognized under the microscope. They are not of much importance in tropical diseases, save in the later stages of blackwater and yellow fever.

Granular casts are composed either of fat or of decomposing protoplasm, and are present in advanced kidney disease which may result from any acute tropical fever.

Amorphous or *hyaline casts* are pale, transparent, and homogeneous, and may be rendered more visible by the addition of iodine. They are believed to be derived from urinary epithelium which has undergone hyaline degeneration. In the early stages of blackwater fever casts of a hyaline nature, formed of coagulated globulin, appear in the urine.

XIII.—SPECTROSCOPIC EXAMINATION OF URINE AND OTHER FLUIDS

The spectroscopic examination of urine, extracts of fæces, and pathological exudates for the presence of recognizable spectra of blood pigments, or their derivatives, may be performed by means of a small direct-vision pocket

Digitized by Google

spectroscope. It is best to examine the urine, or fluid—which, if it contains too much pigment, should be diluted to a suitable degree—in a 6-oz. conical glass, or a test-tube, against a strong light, either artificial or natural. In the tropics, examination in the open air against a white bank of clouds will be found to be most satisfactory. The size of the slit at the objective end should be first regulated so as to obtain the complete and distinct spectrum, then steadily held 1 in. from the glass and gradually moved up and down the entire length of the column of fluid.

If in doubt about the validity of a spectrum, as for instance in watery extracts of fæces or in urine, 100 c.c. should be shaken up well with 20 c.c. of pure amyl alcohol and a few drops of acetic acid. By collecting and filtering the supernatant fluid the intensified spectrum may be obtained.

The spectra, important from a tropical point of view, are those of oxy-hæmoglobin, methæmoglobin, and urobilin in the urine in blackwater fever, malaria, etc., and those of hydrobilirubin and hæmoglobin in the fæces. (Fig. 395.)

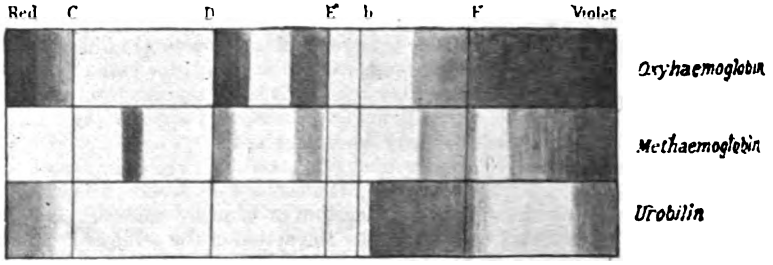


Fig. 395.—Spectra of hæmoglobin and its derivatives.

XIV.—DETECTION OF SPIROCHÆTES, SPIRONES, AND THE GONOCOCCUS

Collection of material. 1. *Superficial lesions.*—The sore or the surface of the lesion should be cleaned up with a piece of cotton-wool soaked in saline or tap-water. It should then be firmly squeezed (preferably by the patient himself) until serum is expressed on the surface; or the sore may be lightly scraped with the edge of a scarifier. If bleeding is caused, it is advisable to wait until it has stopped, as the chances of finding the spirochæte are lessened if blood is present. The serum is best taken up by a capillary pipette, from which it can be distributed on to slides for examination.

2. *Skin lesions.* (*a*) *Papules.*—The superficial layers of epithelium should be removed by scraping with a scarifier, and the serum obtained by squeezing or dry-cupping the papule.

(*b*) *Macules.*—A blister about the size of a threepenny-piece should be applied, the blister fluid removed, and the serum which can be expressed from the raw surface taken for examination.

Detection of spirochætes by dark-ground illumination.—This is the ideal method, and is better than any other for distinguishing one spirochæte from another on morphological grounds. It consists in rendering the microscopic object self-luminous, so that no preliminary treatment

Digitized by Google

is necessary. In order to achieve this, the organism should have a refractility differing from that of the medium in which it lies, and should be illuminated in such a manner that only the light reflected from the object can reach the observer's eye. It is then seen as a bright image on a dark ground. The necessary dark-ground condenser may be fitted to any microscope provided with a mechanical stage and a $\frac{1}{12}$-in. objective.

Metal stop.—This is a funnel-shaped metal tube, inserted into the $\frac{1}{12}$-in. objective with a view to reducing its aperture and the volume of the illuminating rays. The aperture must not exceed 0·95 mm.

The *dark-ground illuminator*, or condenser, of the latest type is paraboloidal; two intense rays of light are made to converge on the object under observation. The best illuminator is that supplied by Leitz.

Cover-glasses and slides.—The slides should be 1 mm. thick, and the cover-glasses No. 1, for use with the Leitz instrument, but the thickness varies with the make of the microscope. All makers state a certain length of tube for which their objectives are corrected, usually 160–170 mm. This is dependent on the thickness of the cover-glass used. The thickness usually allowed for is 0·15–0·18 mm. If the cover-glasses in use are thicker than this, the tube length should be reduced; if thinner, lengthened.

Illuminant.—The selection of a suitable illuminant is a most important point. Wherever obtainable, electric light gives the best illumination, especially the lamp made by the Ediswan Company, known as the "Pointolite." This lamp, fitted with a special hood and adjustable condenser, supplied by Hawksley & Sons (late H. F. Angus & Co.), Wigmore Street, London, is most effective. But apparatus such as the above is not always obtainable in the tropics. Fairly good results may be obtained by using an inverted incandescent gas-burner, but generally the quantity of light available is not sufficiently high. An acetylene bicycle-lamp may also be used with fairly satisfactory results, but in using the substitutes for electric light the rays must always be intensified by means of a strong bull's-eye condenser placed some distance in front of the light.

Manipulation.—Whichever illuminant is used, the microscope should be placed in the vertical position, about 8 in. from the source of light, so that the maximum intensity of the rays may impinge upon the plane mirror. The first step consists in centring the condenser under the low power $\frac{2}{3}$-in. lens; for this purpose it should be racked up to the level of the stage. On focusing it will be observed that the condenser is engraved with two concentric circles which should be accurately centred by means of the screws provided for this purpose. It should then be racked down about an inch below the level of the stage, and a drop of cedar-wood oil, *free from bubbles*, placed on the upper surface of the condenser as well as on the under side of the preparation, and the latter placed upon the stage. When this has been effected, the condenser is gently racked up until the oil comes into contact and spreads evenly upon the under surface of the slide. The observer should then ascertain through the low power that a definite *ring of light* of great intensity illuminates the preparation. At first this appears in the form of a circle with a dark centre, and by manipulating the mirror it can be focused exactly in the centre of the field. The condenser should then be racked up or down, as the case may be, until the black centre is replaced by an evenly illuminated spot. A drop of cedar-wood oil should be placed on the upper surface of the preparation and the $\frac{1}{12}$-in. lens carefully racked down until it comes in contact with the oil. Further focusing should be done with the fine adjustment.

Digitized by Google

Perfect cleanliness is necessary for success; the cover-glasses and slides must be absolutely free from defects and protected from dust.

In order to obtain the best effect the room should be darkened. The microscopic field should be absolutely black, and the spirochætes and micro-organisms should appear as bright specks upon a dark ground.

In order to test the adjustment of the apparatus, a fresh preparation obtained from the mouth or a hollow tooth may be used, in which large numbers of *Spironema dentium* are usually present.

Stained films.—To obtain the best results, it is essential that the film be properly fixed *the moment it dries*, preferably by absolute alcohol or methyl alcohol. The film may then be stained by one of the following methods:

1. *Giemsa's ordinary or long method.*—Cover the slide with a 1 : 10 to 1 : 15 dilution of Giemsa's stain in tap-water and leave for 12 hours. Wash, dry, and examine.

2. *Giemsa's rapid method.*—In this method the same dilution of Giemsa's stain is employed as in the first, only the stain is poured on the slide and the latter held over a flame until the steam rises. This process is repeated three or four times, the last application of stain lasting two minutes. The slide is then washed with water, dried, and examined.

Indian-ink method (Burri).—A drop of the fluid to be examined should be mixed with one drop of indian ink (Pelican brand) on a microscopic slide. This should be spread in a thin layer, as in making a blood-film. The film is then dried in air without the application of heat and, when dry, examined under the $\frac{1}{12}$-in. objective and the spirochætes recognized as white wavy objects on a dark background.

Fontana's method for staining spirochætes in smears.—Smears must be air-dried, not fixed by heat. The fluid, mordant, and stain are as follows:

Hugo's fluid.

Acetic acid	1 c.c.
Formalin	20 „
Aq. dest.	100 „

Mordant.

Tannic acid	5 per cent. in
Carbolic acid	1 „

Silver stain.

Silver nitrate 0·25 per cent. in distilled water. Add ammonia drop by drop until slight turbidity is produced. Excess of ammonia clears the solution and renders it useless.

1. Cover films with Hugo's fluid, flood several times.
2. Wash in water.
3. Cover with mordant. Heat slide till steam rises, and allow to act 30 secs.
4. Wash in water and, without drying,
5. Pour on silver stain. Heat till steam rises. Allow to act 30 secs. Wash in water, dry. The spirochætes are stained brownish to black.

Identification of the gonococcus in stained films.—*Jensen's method* is as follows:

1. Prepare a thin and evenly distributed film from the discharge.
2. Fix the film over a flame, taking care to avoid overheating; this can be guarded against by testing the slide against the back of the hand.

Digitized by Google

3. The preparation should now be allowed to become quite cool.
4. Cover the preparation with a 0·5-per-cent. aqueous solution of methyl-violet (6 B), and allow this to act for a quarter to half a minute.
5. Pour off the methyl-violet as far as possible, and wash away the remainder with a drop or two of strong Lugol's solution (iodine 1 part, potassium iodide 2 parts, distilled water 100 parts). The methyl-violet should *not* be washed off with water.
6. Cover the preparation with a fresh quantity of strong Lugol's solution, and allow this to act for a half to one minute.
7. Wash off the iodine solution with *absolute alcohol*.
8. Cover the preparation with a fresh quantity of absolute alcohol (98 per cent.) and rock the slide as in developing a photographic plate. A further quantity of absolute alcohol may be required to complete decolorization.
9. Finally, rinse the slide with a further small quantity of absolute alcohol and then cover it with a solution of neutral red without any intervening washing in water. Allow the stain to act 15–60 secs. The composition of the neutral-red solution is as follows:—

Neutral red	1 grm.
Aq. dest.	1,000 c.c.
Glacial acetic acid, 1 per cent. . . .	2 „

If this solution of neutral red be found too weak, a stronger one may be employed.

It is recommended that films of known Gram-positive and negative organisms be stained side by side with the material under examination, to serve as controls.

XV.—A PRACTICAL METHOD OF PERFORMING THE WASSERMANN REACTION, SUITABLE FOR THE TROPICS

It is assumed that the student already possesses a knowledge of the theoretical principles upon which this reaction is based, and it is proposed here to deal briefly with the technique step by step.

In the first place it must be remembered that this is essentially a quantitative test and depends upon the interaction of minute quantities of one ingredient with minute quantities of the other; therefore accuracy in measurement of the reagents is essential.

Apparatus required.—*Donald's dropping pipettes* are made to drop definite quantities of fluid, and are graduated by means of the Morse gauge. Three sizes are required, viz.: (*a*) a pipette delivering a drop of 0·02 c.c., (*b*) one delivering 0·05 c.c., (*c*)* one delivering 0·05 c.c. of the alcoholic antigen, which is larger in diameter than (*b*). (Fig. 396.) For further details the reader is referred to Donald's original articles, *Lancet*, 1915, ii. 1243.

Small test-tubes, 2½ in. in length, ⅝ in. in diameter, are the most convenient. The rack for the reception of the tubes and the arrangement of the test should be made with four rows of holes arranged in a serial manner

* This pipette will be referred to as the *antigen pipette*. In order to draw these pipettes from tubing 8 mm. outside diameter, a considerable length, say 10 cm., ought to be heated in a fairly wide blow-pipe flame (for preference the Fletcher burner), and pulled out so that the capillary extremity should be approximately cylindrical. This pipette should preferably be throttled with a spindle-shaped plug to fit into the shoulder.

Digitized by Google

antero-posteriorly. In a lateral direction there should be accommodation for 12 tubes; in other words, the rack should hold 48 altogether. (Fig. 397.)

Reagents. *Sheep's corpuscles.*—Five c.c. of blood are drawn from the jugular vein of a sheep with aseptic precautions. This is added to an equal quantity of sterile citrated saline (0·85-per-cent. NaCl, 2-per-cent. sod. cit.), shaken, and placed in the ice-chest until required.

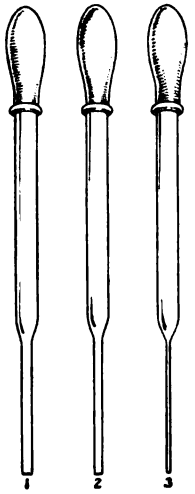


Fig. 396.—Donald's drip pipettes for the Wassermann technique. One-third size.

1, Antigen pipette, 0·05 c.c.; 2, serum pipette, 0·05 c.c.; 3, 0·02 c.c. pipette.

It is a good plan to take two 5-c.c. quantities in case of accident.

To wash the sheep's corpuscles, place in each of four centrifuge tubes 2 c.c. of citrated blood and 8 c.c. of normal saline, then centrifuge. Pipette off the supernatant fluid when perfectly clear, and replace with fresh saline. This process is repeated three times. After the last washing the cells from the four tubes are suspended in saline, so as to make a *6-per-cent. suspension.* The volume of the 6-per-cent. suspension will be determined by the quantity required for the test.

The *complement*, or guinea-pig's serum, is obtained by cutting the animal's throat over a wide glass funnel leading into a centrifuge tube. The blood is allowed to clot, incubated for a short period, and the coagulum separated by means of a platinum wire. The tube should then be centrifuged and *the serum left in contact with the clot for at least six hours before use.* During spells of very hot weather it has been found that the serum of guinea-pigs may, for some unaccountable reason, become deficient in complement. In such circumstances it is advisable to put the animal in the ice-chest for 12 hours before killing it. It will then be found that the blood retains its normal properties.

Patient's serum.—Blood obtained from a prominent vein at the elbow should be collected within 24 hours of performing the test and should not be more than 48 hours old. For the purpose of this test a 1 : 5 dilution of serum is made by adding 0·5 c.c. to 2 c.c. saline; it is inactivated by heating for 15 mins. at 55° C. in a water-bath to destroy complement or any thermolabile anti-complementary body present.

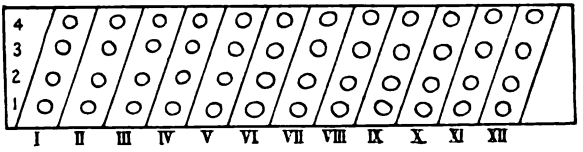


Fig. 397.—Rack for carrying out final Wassermann test.

Antigen may be obtained commercially but does not keep well in the tropics; it is best made from human heart, as follows:—

Solution A.—Fat-free muscular tissue of human heart is ground up in a mortar with a little sand and alcohol. Take 1 grm. to 9 c.c. of absolute

Digitized by Google

alcohol. The solution should be allowed to stand for two or three days, and be shaken from time to time; it should then be filtered through fat-free paper and stored in the ice-chest.

Solution B.—1-per-cent. solution of cholesterin in absolute alcohol. Dissolve with aid of heat and store at room temperature.

For use take—

A, 0·75 c.c.
B, 0·5 ,,
C, 17·5 ,, of normal saline.

Mix A with B, and dilute as quickly as possible with C. This makes a 1 : 15 dilution of antigen, which for the technique to be described is the one usually preferred, though before employing a batch of antigen its *anti-complementary dose* must be ascertained, and not more than one-half of this quantity used in the test. The anti-complementary dose of antigen is the amount that will just fix three minimum hæmolytic doses of complement in the presence of one unit of pooled negative serums.

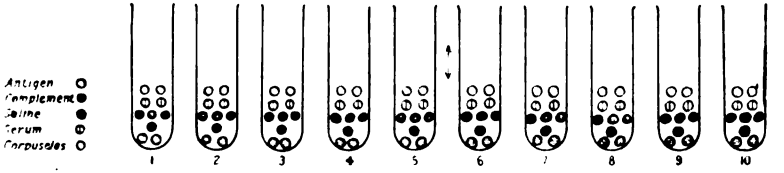


Fig. 398.—Wassermann reaction: titration of antigen.

Method of estimating the anti-complementary dose of antigen.—The following dilutions of antigen should be prepared:—

$\frac{1}{2}$ $\frac{1}{4}$ $\frac{1}{6}$ $\frac{1}{8}$ $\frac{1}{10}$ $\frac{1}{12}$ $\frac{1}{14}$ $\frac{1}{16}$ $\frac{1}{18}$ $\frac{1}{20}$

Arrange a series of tubes in a rack as in Fig. 398, and measure into them from the 0·05 c.c. "antigen pipette"—

ANTIGEN, drops in increasing dilutions:

② ② ② ② ② ② ② ② ② ②

COMPLEMENT, 3 M.H.D.s (p. 917), 0·05 c.c. pipette, drops:

① ① ① ① ① ① ① ① ① ①

SALINE, 0·05 c.c. pipette, drops:

③ ③ ③ ③ ③ ③ ③ ③ ③ ③

POOLED NEGATIVE SERUMS, 0·05 c.c. pipette, drops:

② ② ② ② ② ② ② ② ② ②

Shake the tubes and incubate for one hour at 37° C. Add—

SENSITIZED CORPUSCLES, 0·05 c.c. pipette, drops:

② ② ② ② ② ② ② ② ② ②

Shake the tubes and incubate for 1 hour at 37° C. At the end of this time the readings should be made. Suppose that tubes 1 to 5 show inhibition

Digitized by Google

of hæmolysis whilst tubes 6 onwards show complete hæmolysis, the dose of antigen in tube 5 is the one which shows commencing inhibition of hæmolysis, and is regarded as the anti-complementary unit—i.e. 0·1 c.c. of a 1 : 10 dilution of antigen. *One-half of this is used in the test, 0·1 c.c. of a 1 : 20 dilution.*

Determination of the antigenic unit.—The antigenic unit is that quantity of antigen which just serves to produce complete inhibition of hæmolysis. In conducting the final test, two to four times this unit are used, provided that these amounts are at least four or five times less than the anti-complementary dose.

The titration for the antigenic unit is made in a similar manner to the anti-complementary titration, except that a unit of fresh inactivated serum from a known and untreated syphilitic person is used in place of the known negative in the former case. This test is not absolutely necessary, as about half the anti-complementary dose of antigen is used in the final reaction, which will constitute a good antigenic unit, since the latter is usually very much lower than the anti-complementary dose.

Hæmolytic titration of antigen.—Organic extracts are capable in themselves of hæmolysing red cells; this is due to the hæmotoxic action of lipoids and alcohol. As a general rule, this titration is not absolutely necessary, as, when titrated in the presence of complement, the hæmolytic is higher than the anti-complementary dose, and not more than half of the latter is employed in the final test. It may be conducted with the anti-complementary titration by including more test-tubes in the series and employing higher doses of extract.

The **amboceptor**, or hæmolytic serum, is made by injecting a rabbit intraperitoneally with increasing doses of a 50-per-cent. suspension of washed sheep's corpuscles at weekly intervals. The commencing dose should be 2 c.c., then 5, 7, 10, 15 c.c. After a few weeks the rabbit's serum should be titrated for hæmolytic amboceptor, and when it is sufficiently potent (usually about ten days after the sixth injection) the rabbit is bled to death. The serum is collected in a sterile manner and stored in ampoules. After bottling, complement should be removed by heating for half an hour at 55° C. It may be kept in the ice-chest for months without deterioration. An amboceptor of lower titre than 1 : 1,000 should not be used.

This reagent may also be obtained commercially, but experience has shown that amboceptor sent out from England to the tropics greatly deteriorates in titre.

Sensitization of sheep's corpuscles.—The corpuscular suspension should be sensitized by adding 4–5 M.H.D.s of amboceptor, *the minimum hæmolytic dose being that quantity which just serves to produce complete hæmolysis in one volume of a 3-per-cent. suspension of corpuscles in the presence of 3 M.H.D.s of complement after incubation for one hour at 37° C.* It is determined as follows: A series of test-tubes is set up in a row as in titration of antigen. Place in each tube one volume of a 3-per-cent. suspension of sheep's cells. A series of dilutions of the amboceptor should now be prepared—e.g. 1 : 125, 1 : 250, 1 : 500, 1 : 750, 1 : 1,000, 1 : 1,500, 1 : 2,000, and one volume of each dilution added to each tube in turn. The row of tubes now contains a series of equal quantities of sheep's corpuscles in contact with varying quantities of hæmolytic amboceptor. After half an hour, add 3 M.H.D.s of complement to each tube, followed by saline to make the final volume the same as that of the test itself. Incubate for one hour at 37° C., shaking the tubes from time to time. The final readings should be made

Digitized by Google

at the end of the hour. The tube is selected which contains the smallest quantity of amboceptor in which hæmolysis is complete. The dilution of amboceptor in this tube represents the minimum hæmolytic dose of the titrated amboceptor.

Assuming that the tube containing the 1 : 1,500 dilution of amboceptor is selected as containing the M.H.D., and that 20 c.c. of sensitized cells are required for titration of complement and for the test, then, by adding 10 c.c. of a 6-per-cent. suspension of sheep's cells to 10 c.c. of a 1 : 150 dilution of the amboceptor, 20 c.c. of a 3-per-cent. suspension of cells and a 1 : 300 dilution of amboceptor, which represents 5 M.H.D.s, are obtained.

Every fresh batch of amboceptor should be titrated as described above, before use, and at frequent intervals afterwards when working in the tropics.

After adding the amboceptor the flask containing the cells should be placed in the incubator for half an hour, afterwards in the ice-chest until required for use.

Before proceeding with the test proper, the complement must be titrated with a view to determining the M.H.D. (*the minimum hæmolytic dose*), i.e.

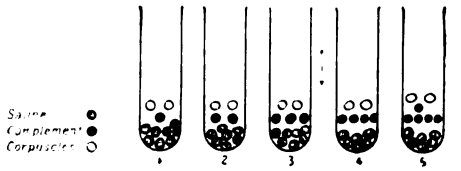


Fig. 399.—Wassermann reaction: titration of complement.

that quantity of complement which just serves to produce complete hæmolysis in one volume of a 3-per-cent. suspension of sheep's corpuscles in the presence of 4–5 M.H.D.s of amboceptor after incubation for one hour at 37° C. It is estimated as follows:—

Set up a series of tubes in a rack in the manner shown in Fig. 399:—

Add—

1. SALINE, 0·05 c.c. pipette, drops:

⑧	⑦	⑦	⑥	⑥

2. COMPLEMENT, 1 : 60 dilution, 0·02 c.c. pipette, drops:

①	②	③	④	⑤

3. SENSITIZED CORPUSCLES, 0·05 c.c. pipette, drops:

②	②	②	②	②

The tubes should be shaken, then incubated for one hour at 37° C. It is a good plan to shake the tubes three or four times during the incubation period. Suppose that at the end of one hour Nos. 4 and 5 tubes show complete hæmolysis, whilst in Nos. 1, 2, and 3 hæmolysis is inhibited, then four drops of a 1 : 60 dilution of complement from the 0·02 c.c. pipette = 0·08 c.c. may be regarded as the M.H.D. and 0·08 c.c. of a 1 : 20 dilution will therefore be 3 M.H.D.s, and is the quantity to be used in the final test. In the final test a dilution of serum 0·05 c.c. of which represents 3 M.H.D.s of

Digitized by Google

complement is employed for convenience. The following calculation will show the dilution of guinea-pig's serum to make:

4 drops from 0·02 c.c. pipette = 0·08 c.c. of 1 : 60 guinea-pig's serum = 1 M.H.D., as determined by above titration. Then 0·08 c.c. of 1 : 20 serum = 3 M.H.D.s, and 0·05 c.c. of a $\frac{20}{8} \times 5 = \frac{100}{8}$ = 1 : 12·5 dilution = 3 M.H.D.s.

Having determined the M.H.D. of complement and having made a convenient dilution, the test proper can now be carried out.

The rack described (Fig. 397) should be fitted with test-tubes. The rows marked in Roman numerals from I–XII each comprise a set of 4 tubes. These are numbered 1–4 in an antero-posterior direction, and represent the test of each patient's serum. In interpreting Fig. 400 and the explanatory text to follow, the reader should remember that the tubes labelled 1–4 should be read as if they were placed in the rack as indicated above. The

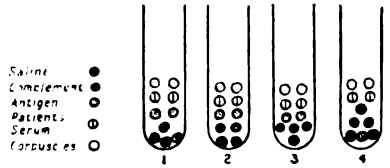


Fig. 400.—Wassermann reaction: showing composition of final test.

object in using a rack in which the holes are arranged on the slant is to enable one to see all the four tubes in each set at one glance without moving the rack about.

Add to each tube in an antero-posterior direction the following drops:—

SALINE, 0·05 c.c. pipette, drops:

③ ② ① ⑤

COMPLEMENT, in required dilution, 3, 6, and 9 M.H.D.s, i.e. 0·05 c.c. pipette, drops:

3 M.H.D.s 6 M.H.D.s 9 M.H.D.s ¾ M.H.D.s.

① ② ③ ①

ANTIGEN, 0·05 c.c. "antigen pipette" = ½ anti-complementary dose, drops:

② ② ② ⓪

PATIENT'S SERUM, 1 : 5 inactivated, 0·05 c.c. pipette, drops:

② ② ② ②

Shake the tubes and incubate for one hour at 37° C., then add—

SENSITIZED CORPUSCLES, 0·05 c.c. pipette, drops:

② ② ② ②

Incubate for a further period of one hour. The tubes should be shaken every quarter-hour, and the tests read to see that the reaction is proceeding

Digitized by Google

satisfactorily. The final readings should be made at the end of one hour.

Recording of results.—A P + + + indicates an entire absence of hæmolysis in tubes 1, 2, and 3, and should be registered as a strongly positive reaction. A P + + means that there is an entire absence of hæmolysis in tubes 1 and 2, and is a definitely positive reaction. A P + reaction indicates an absence of hæmolysis in tube No. 1, and is regarded as positive in the presence of suggestive clinical evidence of the disease or in a treated case. A P ± means partial hæmolysis in tube No. 1, and serums giving such reactions should be retested at a subsequent date. It is best to complete the addition of each reagent to the whole series of tubes at one operation. Thus, in the final test, the addition of saline to all tubes is completed before proceeding to add the complement, and so on. Care must be taken to wash out the pipette after completing the addition of each solution.

In adding the inactivated serum of the patient, *great care* must be taken to add each serum to its corresponding series of tubes in the rack. It is well to wash out the pipette (1) with cold water, (2) with *boiling* water, and (3) with saline, after adding each specimen of serum.

It will be noted that the total volume of reagents in the final test is 0·5 c.c., each individual volume approximating 0·1 c.c. It is important, in making titrations, to determine, for instance, the M.H.D. of complement, amboceptor, and the anti-complementary dose of antigen, that the final volume of reagents should be 0·5 c.c., so as to correspond with the volume used in the actual test.

In addition to the serums under examination, a *known positive* and *negative serum* should always be included in the test.

It will be seen that the fourth row of tubes contains only serum, saline, complement (3 M.H.D.s), and corpuscles, the antigen being omitted; this serves to detect the presence of any anti-complementary tendency in the serum under examination.

Antigen and complement controls are included in the final test, and are put up as follows (Fig. 401):—

Add to each tube in an antero-posterior direction—

SALINE, 0·05 c.c. pipette, drops:

⑤ ③ ⑦

COMPLEMENT, 3 M.H.D.s, 0·05 c.c. pipette, drops:

① ① ①

ANTIGEN, 0·05 c.c. "antigen pipette," drops:

② ④ ⓪

Incubate one hour at 37° C., then add—

SENSITIZED CORPUSCLES, 0·05 c.c. pipette, drops:

② ② ②

No. 1 tube contains the same dose of antigen as in test; No. 2 contains a double dose; while No. 3 contains saline, complement, and corpuscles alone. If the reaction is proceeding satisfactorily, all these control tubes should show complete hæmolysis.

Digitized by Google

A corpuscle control may also be included, i.e. a volume of the corpuscles in saline; this should show no hæmolysis.

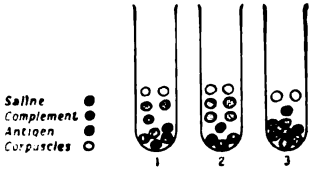


Fig. 401.—Wassermann reaction: showing antigen and complement controls, used in final test.

XVI.—FIXATION OF TISSUES FOR PARAFFIN SECTIONS

Fixation by formalin.

Formalin	10 parts
Water	90 ,,

1. Trim specimens to a suitable size for embedding ½ in. square; wash in normal saline.
2. Fix for about 12 hours.
3. Wash in running water for 24 hours.
4. Place in 60 per cent. alcohol, in which they can be stored indefinitely.

Fixation by Zenker's fluid.—This method is employed for the demonstration of protozoa and tissue changes.

Bichromate of potassium	2·5 grm.
Corrosive sublimate	5 ,,
Water	100 c.c.
Glacial acetic acid	5 ,,

Dissolve the corrosive sublimate and the bichromate of potassium in the water with the aid of heat. The acetic acid should be added in the proper proportion to the quantity of fluid taken for fixing purposes, and not to the stock solution, as the acid evaporates rapidly and also produces changes in the chrome salt. Sodium sulphate is omitted, as it serves no useful purpose.

1. Fix tissues for 12–24 hours.
2. Wash in running water. 12–24 hours.
3. Place in 80-per-cent. alcohol until required for use.

Fixation by mercuric chloride.—This method may be employed when Zenker's fluid cannot be procured. It is especially suitable for detection of fine changes in tissues, pigments, and protozoa.

1. Trim specimens to a suitable size for embedding, about ½ in. square, and wash in normal saline.
2. Fix in a saturated solution of mercuric chloride in normal saline, with the addition of a few drops of glacial acetic acid, for 12–24 hours.
3. Wash in running water for 24 hours; it is a good plan to tie up the specimens into a small bag made of gauze, so as to prevent them from being washed away and to keep them identified.
4. Place in 50-per-cent. alcohol rendered sherry-wine colour by addition of Weigert's iodine. The perchloride is removed by the iodine, a process which usually takes more than 24 hours. It is characterized by

Digitized by Google

the discoloration of the iodine and should be continued until this no longer takes place. It is a good plan to slice the specimen half through with parallel cuts about ¼ in. apart to enable the iodine to permeate rapidly.

5. Wash and place in hyposulphite-of-soda solution (a few crystals in water) to remove all traces of iodine.
6. After washing out the hyposulphite with water, the specimens may be stored indefinitely, and transmitted to England for further examination, in 60-per-cent. alcohol.

Fixation of intestines.—In fixing small pieces of bowel, it is a good plan to lay the specimen, while wet, peritoneal side downwards, on a piece of thick dry filter-paper; this prevents the specimen from becoming curled up. The whole is put into the fixing fluid, and the paper removed after fixation. The number or name of the specimen may also be written on the paper.

Embedding in paraffin wax.—The piece of fixed tissue is washed in running water for 12 hours and transferred as follows:

1. 50-per-cent. alcohol, 12 hours.
2. 70-per-cent. alcohol, 12 hours.
3. Absolute alcohol (1), 12 hours.
4. Absolute alcohol (2), 12 hours.
5. Xylol or chloroform (1), 12 hours.
6. Xylol or chloroform (2), 12 hours or until perfectly clear.
7. Xylol or chloroform and soft paraffin, equal parts, 12 hours.
8. Fresh soft paraffin, 12 hours.
9. Hard paraffin, 56–60° C., 12 hours.
10. Embed in hard paraffin.

If L blocks are unobtainable the bottom of a syringe case smeared with glycerin makes a useful mould.

An improvised paraffin bath may be made out of a closed kerosene tin provided with a water-jacket, such as can be made by a native tinsmith. The bath is heated by one or more spirit lamps, and the temperature can be regulated by placing the flames at varying distances from the bottom of the bath. Such an apparatus requires constant supervision and must not be left overnight. For continuous paraffin work it is essential to have a proper apparatus with a regulated flame. For infiltration of the paraffin the specimens are best placed in small specimen-tubes 3 in. by 1 in.

Cutting and mounting paraffin sections of tissues.—It is unnecessary to describe all the various stages of section-cutting in detail, except to advise measures especially applicable to the tropics.

To prevent them from becoming too soft, the blocks of paraffin containing the tissues should be stored in cold water to which ice, if procurable, has been added. In trimming the blocks after affixing to the object-holder, great care should be taken that the upper and lower edges are parallel to one another, and that a sufficient margin is left between the limits of the tissue and the edges of the block.

In cutting, a hollow-ground razor should not be used, as it is too resilient; a plain heavy blade, if *stropped before and after use*, answers the purpose admirably.

When using the "Cambridge" rocker—the best instrument for paraffin sections in the tropics—the resulting sections should be as thin as possible; that is to say, the "cut" should be regulated to the third notch on the indicator.

Digitized by Google

After a ribbon has been cut, a camel's-hair brush is used for transferring it to water kept a few degrees below the melting-point of the paraffin employed. The ribbons should be laid flat with their glossy surface towards the water.

The most satisfactory method of mounting on slides consists in dividing the ribbon into suitable portions by means of a hot knife and then floating them on to a clean slide. Unless properly fixed, the sections are apt to curl in subsequent manipulations. Some consider it advisable for this purpose to affix by means of an egg-albumen solution slightly smeared upon the recipient slide (equal parts of egg-albumen and glycerin with a small crystal of thymol). However mounted, they should be drained by means of blotting-paper and held for a few seconds over a flame or, better still, over steam from boiling water, in order that they may settle down evenly upon the slide.

Having been in the incubator for half an hour at 37° C., in an oblique position, the sections may be proceeded with—that is, if fixed with egg-albumen: if not, they must be left for at least 12 hours.

Staining paraffin sections.—For general work the *hæmatoxylin and eosin* method is to be recommended.

1. Pass sections through xylol and alcohols to water.
2. Stain 15–30 mins. with hæmatoxylin (Ehrlich's).
3. Blue in water.
4. Wash for 1 min. in acid alcohol—70-per-cent. alcohol 100 c.c., HCl 1 c.c.
5. Blue again in water.
6. Counterstain for 2 mins. in watery eosin (sat. sol. eosin in H_2O).
7. Wash with 70-per-cent. alcohol till no more colour comes away.
8. Wash in two changes of absolute alcohol.
9. Dehydrate in xylol.
10. Mount in Canada balsam.

NOTE.—Mayer's acid hæmalum may be used in place of hæmatoxylin, if good nuclear structure is to be shown, e.g. amœbæ in tissue, etc. If this stain is used, treat only for 15 mins. and do not use the acid alcohol. Saturated alcoholic solution of orange or Van Gieson may be substituted for the watery eosin.

Weigert's iron hæmatoxylin and Van Gieson.—This stain is recommended for showing the details of nuclear structure, connective tissue, and collagen fibres; it also gives a beautiful differentiation of amœbæ.

1. Pass sections through xylols and alcohols to water.
2. Stain 10 mins. with Weigert's hæmatoxylin.
3. Wash in tap-water till black, say 20 mins.
4. Differentiate thoroughly in acid alcohol.

This takes 1–2 mins.; it is difficult to overdo it—hæmatoxylin will remain firm in the nuclei.

5. Wash in tap-water till a delicate grey colour is obtained.
6. Stain in Van Gieson for 1½ mins.
7. Dip rapidly in tap-water to differentiate the Van Gieson.
8. Dehydrate with absolute alcohol.
9. Clear with xylol.
10. Mount in Canada balsam.

Method of using Giemsa stain for paraffin sections.—To demonstrate

Digitized by Google

protozoa this stain may be employed. Gauducheau's stain (p. 882) may be used in the same manner.

1. Remove the paraffin wax from thinly cut sections.
2. Obtain a Petri dish and fit in two pieces of glass rod.
3. Put the sections surface downwards into the dish.
4. Pour in Giemsa solution (Giemsa 1 part, distilled water 9 parts) and leave for 24–48 hours.
5. Differentiate with *acetone* 95 c.c., xylol 5 c.c.
6. Wash in acetone 70 c.c., xylol 30 c.c.
7. Wash in acetone 30 c.c., xylol 70 c.c.
8. Wash in acetone 5 c.c., xylol 95 c.c.
9. Clear in xylol and mount in Canada balsam.

Weigert-Gram method for fibrin and bacteria in sections.—This method is carried out as follows:

1. Pass sections through xylols and alcohols to water.
2. Stain with lithia carmine solution for 10–30 mins.
3. Differentiate rapidly in acid alcohol; rinse in 70-per-cent. alcohol.
4. Stain with aniline gentian violet for 5 mins.
5. Remove excess of stain and pour on Weigert's iodine; allow to act for 10 mins.
6. Dry with blotting-paper.
7. Differentiate with aniline oil and xylol till no more blue comes away.
8. Clear with xylol.
9. Mount in Canada balsam.

Levaditi's method for demonstration of spirochætes in tissues.

1. Small pieces of suspected tissue are placed in 10-per-cent. formalin and left for 48 hours.
2. Wash in running water for 12 hours.
3. 96-per-cent. alcohol for 24 hours.
4. Distilled water till tissues sink.
5. Silver nitrate 1·5 per cent. for 3–5 days in incubator at 37° C.
6. Wash rapidly in water.
7. Place at room temperature for 24 hours in a solution of

Pyrogallic acid	2 grm.
Formalin	5 per cent.
Distilled water	100 c.c.

8. Wash well in water for 12 hours.
9. Pass through alcohols and xylols to paraffin wax.
10. Embed in paraffin wax.
11. Cut thin sections, mount, dry, clear with xylol, and mount in Canada balsam.
12. The spirochætes are seen stained deep black on a brown background.

Dobell's modification of Levaditi's method.*—The important points about this method are that the formalin must be thoroughly washed out with alcohol, and the latter removed completely with distilled water before immersing in the silver solution.

* We are indebted to Prof. Clifford Dobell, F.R.S., for permission to publish this method.

Digitized by Google

1. Tissues fixed in 10-per-cent. formalin for 24 hours or longer.
2. Harden in absolute alcohol for 24 hours.
3. Keep in 70-per-cent. alcohol.
4. Reduce alcohol gradually to distilled water.
5. Put into ¼–½-per-cent. solution silver nitrate for 18–24 hours in incubator at 37° C.
6. Wash thoroughly in distilled water to get rid of the silver.
7. Put into ½–1-per-cent. solution hydroquinone in distilled water (i), or 50-per-cent. solution of alcohol (ii), and leave for 18–24 hours.
8. Wash in low alcohols if (i), or 70-per-cent. alcohol if (ii).
9. Dehydrate. Absolute alcohol, chloroform, paraffin wax.
10. Cut and stain with hæmatoxylin and eosin, or any other method required.
11. The spirochætes only are stained black.

XVII.—PRESERVATION OF TISSUES FOR MUSEUM PURPOSES, IN ORDER TO RETAIN THEIR NATURAL COLOURS

The following method is recommended for the tropics.

If it is necessary to remove fæces from the specimens, they should be washed in normal saline.

Fix in No. 1 Kaiserling solution:

Formalin	200 c.c.
Nitrate of potassium	15 grm.
Acetate of potassium	30 „
Water	1,000 c.c.

The length of time required for fixation depends upon the nature and thickness of the specimen. In the case of thin bowel, leave 1–2 hours; for thick bowel, 3–6 hours will be required. In order to prevent the intestine from shrinking, the specimen should be pinned out flat, with drawing-pins, on a piece of wood before placing it downwards in the fixing solution. After fixing, it should be trimmed up to make a good museum specimen.

In the case of solid organs, the vessels should be injected with Kaiserling solution, or 2–5 c.c. injected into the pulp, here and there, by means of a syringe. In this case fixation takes 24–72 hours, depending entirely upon the size of the specimen.

It is a good plan to test the completeness of fixation by means of a needle. After a little experience, the exact amount of resistance offered by a correctly fixed specimen is easily judged.

After fixation, the specimen should be drained and placed in 80-per-cent. alcohol for about 4 hours, then in rectified spirit for about ½ hour. Too long immersion in alcohol tends to *bleach* the colours, therefore the specimens should be well watched at this stage. The 80-per-cent. alcohol restores the natural colours, and the rectified spirit fixes them. A solid organ will require several days, the exact time needing a considerable amount of practical experience to determine.

Preserve finally in No. 2 Kaiserling solution:

Potassium acetate	200 grm.
Glycerin	400 c.c.
Water	2,000 „

Filter the potassium acetate before adding the glycerin. Great care

Digitized by Google

must be taken that this solution is *acid-free*. It is advisable to add camphor or thymol 1 per cent. to prevent the growth of moulds.

In this solution specimens well wrapped in cotton-wool keep indefinitely and may be transmitted to any part of the world. For identification it is important that numbered bone discs should be used, and they should be affixed by string, and not by wire, which rusts.

XVIII.—METHODS OF REARING, DISSECTING, AND PRESERVING MOSQUITOES

Collecting.—Hibernating mosquitoes required for experimental work are easily collected with the aid of a glass bottle (a pickle bottle serves admirably), through the cork of which the upper half of an ordinary test-tube is inserted (*see* Fig. 402). The tube is held directly over the mosquito and gently moved aside, so as to disturb the resting insect, which immediately flies down the tube into the bottle. A cotton-wool plug is inserted to prevent escape (over 100 mosquitoes have been caught in one of these containers on a single occasion).

A piece of blotting-paper in the bottle acts as a perch for the mosquitoes; they might otherwise be damaged by the water of condensation which collects if the bottle be held in the hand for any length of time. The insects remain alive in this container for several hours, but it is advisable to cage them as soon as convenient.

Caging.—A convenient cage may be made from a small wooden box about 1½ ft. by 1 ft. The bottom is removed and the sides are used as roof and floor. One end is taken out, and from it two strips 1 in. wide are cut, and nailed at the bottom end, to support the roof and floor. A sheet of white paper is then gummed to the floor. At both sides mosquito-netting is attached and stretched, being held in position with gum or seccotine. The edges of the netting are further strengthened by tacking on strips of brown paper or tape. The open end of the cage is then fitted with a linen sleeve, one end being tacked on and strengthened with paper or tape. The open end of the sleeve is fastened with tape. A stand may now be made, the legs of which are placed in small basins of cresol to prevent the access of ants. (Fig. 403.) A basin of fresh water containing some floating grass is placed inside the cage, in which the insects may deposit their eggs. A little liquid glucose on a pad of cotton-wool placed on a gauze-covered aperture in the roof of the cage serves admirably as a source of food. The insects imbibe the liquid from underneath, and do not become soiled thereby. The pad should be renewed daily. Food should not be placed inside the cage. Before depositing ova a feed of mammalian blood appears to be necessary. A tame rabbit may be conveniently utilized for this purpose. When required, individual insects are readily removed from the cage with the aid of a test-tube. Considerable difficulty will be experienced in rearing the larvæ of anopheles from the eggs deposited by the adult insects. In order to do so, an effort should be made to obtain the natural water from the ditches and swamps in which these insects breed, and also a supply of *confervæ* and *spirogyra* upon which the larvæ feed. The atmosphere in the cage must be kept warm and moist.

Dissection.—After killing the mosquito with chloroform the legs and wings should be removed, and the body placed on a slide containing a drop of normal saline. Put the slide under a dissecting microscope, and with the

Digitized by Google

aid of two fine surgical needles mounted in wooden handles carefully remove the head by holding the thorax with one needle and gently exerting traction on the head with the other. The salivary glands are generally adherent to the head and can be "snicked" off. If such is not the case, carefully remove a portion of the chitinous surface of the thorax; then, by fixing the lower part with one needle, the protruding glands are gently withdrawn with the other. To remove the stomach, "snick" each side of the last abdominal segment, grasping the upper part of the abdomen with the left needle, and withdraw the viscus with the right. The stomach and salivary glands, which must not be allowed to dry, are then covered with a cover-slip and examined under a low power of the microscope. After a little practice no difficulty will be experienced in recognizing the spherical, refractile

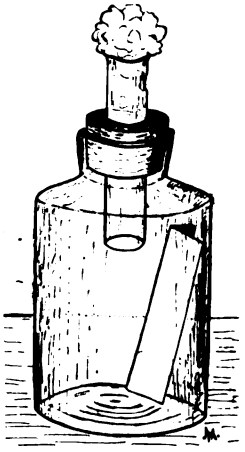


Fig. 402.—Bottle for collecting live mosquitoes. (*A. Michieli.*)

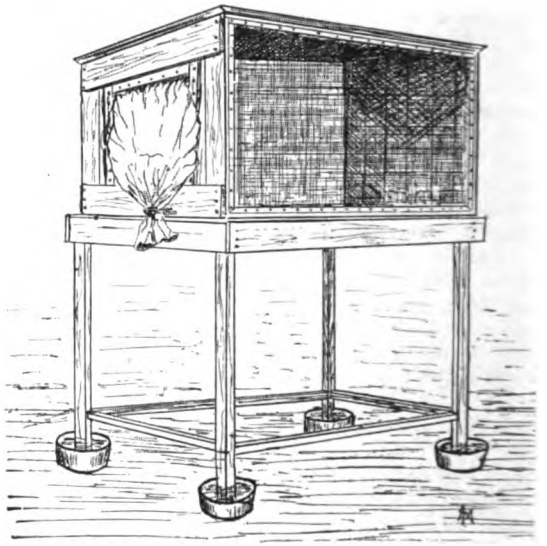


Fig. 403.—Cage for rearing and storing living mosquitoes. (*A. Michieli.*)

oöcysts of the malaria parasite containing pigment and protoplasmic masses, and in distinguishing them from "pancreatic cells," gregarines, and even encysted trematodes, which are found in the stomach of anopheles from time to time.

In the examination of the salivary glands, special care must be taken not to confuse certain crystals, which occur in many anophelines, with sporozoites. These crystals are only slowly dissolved in the saline, but disappear at once with the application of 1 per cent. of any of the mineral acids (Wenyon).

Mounting.—Various methods of mounting mosquitoes have been described, but perhaps the simplest is the cardboard disc method. Good results can only be obtained if the fly has been recently killed. (It is possible to obtain fair results with insects that have been dead for some time, if they are relaxed

Digitized by Google

by placing them for 24 hours in a tube containing cotton-wool soaked in 70-per-cent. alcohol provided with a stopper soaked in the same solution.)

The specimen for mounting is laid on its back on a sheet of cork. A fine entomological pin is then gently pushed through a circular cardboard disc, with the aid of entomological forceps, so that half the pin protrudes on either side. The sharp end is pushed through the centre of the thorax. The pin is then gently pulled down so that the insect lies flush with the card. With the aid of a mounted needle the legs are carefully arranged; this done, a larger pin is inserted into the top of the disc, and in this manner the disc is pinned into a storing box.

Before the mounting is done, the species of insect, locality, date, etc., should be neatly written on the under surface of the disc for reference. If the specimens are to be sent a long distance, the bottom of the storing box should be lined with sheet cork fixed into position with equal parts of melted paraffin wax and naphthaline.

A cigar-box, the bottom of which is covered with dental wax, or fitted with sheet cork as above, serves admirably as a storing box for mosquitoes. If naphthaline is not used, a piece of cotton-wool soaked in creosote and pinned into a corner of the box will prevent the growth of moulds.

Very useful mounts may be made for mosquitoes by constructing a cell out of paraffin wax on an ordinary glass slide, arranging the mosquitoes in position, and covering with a cover-slip in position by melting the edges of the wax with a hot knife or needle. Such specimens may easily be carried about in a slide box, and examined when required under a low power of the microscope.

Transportation.—Though it is better to pin out all insects before sending home for identification, they may be transmitted as follows: A layer ½ inch thick of naphthaline crystals should be placed at the bottom of a test-tube and covered with a thin layer of cotton-wool. Two or three specimens are dropped on this, and held in position by a plug of wool. More insects and wads of cotton may be inserted till the tube is full. Finally the tube can be corked, or sealed with paraffin.

Mosquitoes to be sent home for section should be dropped alive into a tube of 70-per cent. alcohol and transmitted in this fluid.

Celloidin sections.—In order to obtain satisfactory microscopic sections of mosquitoes they must be cut in celloidin. To do this the following points must be observed:

1. Drop alive into 70-per-cent. alcohol.
2. Remove legs and wings 24 hours after.
3. Place in fresh alcohol 90 per cent., 24 hours.
4. Ether and alcohol (equal parts), 24 hours.
5. Thin celloidin (dissolved in ether and alcohol, equal parts), 24 hours.
6. Thick celloidin, 24 hours.

In order to mount, pour thick celloidin on the surface of a wooden block, allow a skin to form, drop the mosquito in lightly and allow it to sink and set thoroughly, then put into 60-per-cent. alcohol and leave for 12 hours.

Cut sections on a sliding microtome provided with a large sharp blade, and with the aid of a camel's-hair brush remove the sections from the razor (which should be kept wet), float in spirit, and wash in water several times.

1. Stain with acid hæmatoxylin (Ehrlich's), 10–15 mins.
2. Blue in water.
3. Wash for 1 min. in 1-per-cent. acid alcohol.

Digitized by Google

4. Blue again in water.
5. Counterstain with watery eosin, ½ min.
6. Wash rapidly through alcohols 40 per cent., 70 per cent., and 90 per cent.
7. Leave for 10 mins. in 90-per-cent. alcohol.
8. Clear in carbol xylol (30-per-cent. phenol in xylol).
9. Leave in fresh carbol xylol for 15 mins.
10. Mount in Canada balsam.

The mosquitoes, from the beginning of the process, must not be allowed to dry. Neither absolute alcohol nor clove oil can be used.

Mosquitoes may be preserved for section in glycerin. Some observers prefer this method.

Paraffin sections.—Stomachs of mosquitoes containing malaria oöcysts can be cut into serial sections if required. Slip from the slide the portions found to be infected into a watch-glass containing Schaudinn's fluid (alcohol 1 part, saturated corrosive sublimate 2 parts, 1-per-cent. acetic acid), leave to fix for 15–30 mins.

1. Wash thoroughly with several changes of alcohol 70 per cent.
2. Leave in absolute alcohol, and change several times till water has been removed.
3. Clear in xylol.
4. Put a watch-glass full of paraffin wax on a sand-bath over a low Bunsen flame and keep it at a temperature of under 60° C.
5. Transfer the specimens from the xylol and leave in paraffin wax about 1 hour.
6. Remove the watch-glass.
7. Allow the wax to set thoroughly.
8. Trim the block up.
9. Cut sections on rocking microtome and arrange in series on a slide covered with egg-albumen.
10. Leave in incubator for 24 hours to dry.
11. Remove the mercury with iodine, and the iodine with hyposulphite-of-soda solution.
12. Stain with hæmatoxylin and eosin.

Recently Wenyon has improved upon this method by staining the tissue *en masse* in diluted Mayer's acid hæmalum for 12 hours, after fixation. Subsequently the tissue is embedded in paraffin and cut as described above.

To obtain sections of the salivary gland, dissect out the contents of the thorax after removal of the head. The muscular mass containing the gland is fixed and treated as above.

XIX.—FORMULÆ OF STAINS COMMONLY IN USE

Löffler's methylene-blue.—A bacterial stain.

Saturated alcoholic solution of methylene-blue	30 c.c.
Solution of KOH in aqua destillata (1 : 10,000)	100 „

This solution is conveniently made by adding 1 c.c. of a 1-per-cent. solution to 99 c.c. of water.

Ziehl-Neelsen carbol fuchsin.—For acid-fast bacilli.

Basic fuchsin	1 part
Absolute alcohol	10 parts
1 : 20 carbolic-acid solution	100 „

Digitized by Google

Neisser's stain.—For diphtheria bacilli.

A. Dissolve 1 grm. of methylene-blue in 20 c.c. of 96-per-cent. alcohol, and to the solution add 950 c.c. of distilled water and 50 c.c. of glacial acetic acid.

B. Two grm. of Bismarck brown are dissolved in 1 litre of distilled water.

Films are stained in A for 1–3 secs., washed in water, and stained for a further 3–5 secs. in B; they are then dried and mounted.

Borax methylene-blue.

Methylene-blue	2 grm.
Borax	5 ,,
Water	100 c.c.

Methylene-blue, watery.

Saturated solution of methylene-blue in water. Dilute as required.

Aniline gentian-violet.

Aniline oil	4 c.c.
Aqua destillata	96 ,,

Mix thoroughly and add 10 c.c. of saturated alcoholic solution of gentian-violet.

Archibald's stain for plague.

No. 1— *Stock Solutions*

Thionin	0·5 grm.
Phenol crystals	2·5 ,,
Formalin	1·0 c.c.
Aq. destil.	100·0 ,,

No. 2—

Methylene-blue	0·5 grm.
Phenol crystals	2·5 ,,
Formalin	1·0 c.c.
Aq. destil.	100·0 ,,

Dissolve for 24 hours.

Before use, mix equal parts of No. 1 and No. 2 and filter.
Fix film by heat and stain for 10 secs.
Wash and dry.

Stains used for Paraffin Sections

Delafield's hæmatoxylin.

Hæmatoxylin crystals	4 grm.
Alcohol 95 per cent.	25 c.c.
Saturated aqueous solution of ammonia alum	400 ,,

Dissolve the hæmatoxylin in the alcohol and add the alum solution. Expose the mixture to light and air in an unstoppered wide-neck bottle for 3 or 4 days. Filter, and add—

Glycerin	100 parts
Alcohol 95 per cent.	100 ,,

Digitized by Google

Allow solution to stand in the light until it assumes a deep purple colour. Filter, and keep in a well-stoppered bottle.

Weigert's iron hæmatoxylin.

A.	Hæmatoxylin	1 grm.
	Alcohol 96 per cent.	100 c.c.
B.	Liq. ferri perchloridi (30 per cent.)	4 ,,
	Hydrochloric acid conc.	1 ,,
	Water	100 ,,

Keep solutions in separate bottles. Allow A to ripen before use. Just before the stain is to be used, mix equal parts of A and B. The mixture does not keep for more than a few days.

Lithia carmine.

Carmine	2·5 grm.
Lithia carbonate	5·0 ,,
Water	100 c.c.

Hæmatoxylin (Ehrlich's).

Hæmatoxylin	2·5 grm.
Absolute alcohol	50 c.c.
Potash alum	50 grm.
Distilled water	1,000 c.c.

The hæmatoxylin is dissolved by heat in absolute alcohol in a test-tube, and the alum, also by heat, in water in an evaporating basin. The two solutions are added together in a clean bottle. The resulting solution is placed in strong sunlight and left until the sides of the container are stained deeply. In the tropics this takes but a few days. A crystal of thymol is added to prevent the growth of moulds.

Van Gieson's picro-fuchsin.

1-per-cent. aqueous solution of acid fuchsin	5 c.c.
Saturated aqueous solution of picric acid	100 ,,

Mayer's hæmalum.—A hæmatoxylin stain for tissues.

Hæmatoxylin crystals	1 grm.
Distilled water	1,000 c.c.

Dissolve, and add—

Iodate of sodium	0·2 grm.
Potash alum	50 ,,
Chloral hydrate	50 ,,
Glacial acetic acid	20 c.c.

The stain is ready for use as soon as the ingredients have dissolved.

SOLUBILITIES OF THE COMMONER STAINS

100 c.c. saturated	aqueous	methylene-blue	contains	0·66 grm.	stain.
,, ,,	alcoholic	,,	,,	6·68 ,,	,,
,, ,,	aqueous	gentian-violet	,,	1·75 ,,	,,
,, ,,	alcoholic	,,	,,	4·42 ,,	,,
,, ,,	aqueous	basic fuchsin	,,	0·66 ,,	,,
,, ,,	alcoholic	,,	,,	2·92 ,,	,,

Digitized by Google

XX.—SCALES AND STANDARDS

Centigrade and Fahrenheit scales.—To convert Fahrenheit into Centigrade, subtract 32, multiply the remainder by 5, and divide the result by 9.

To convert Centigrade into Fahrenheit, multiply by 9, divide by 5, and add 32.

The following table and figure show the relation of Fahrenheit to Centigrade degrees.

Centigrade.	Fahrenheit.	Centigrade.	Fahrenheit.
110°	230°	37°	98·6°
100	212	36·5	97·7
95	203	36	96·8
90	194	35·5	95·9
85	185	35	95·0
80	176	34	93·2
75	167	33	91·4
70	158	32	89·6
65	149	31	87·8
60	140	30	86
55	131	25	77
50	122	20	68
45	113	15	59
44	111·2	10	50
43	109·4	+ 5	41
42	107·6	0	32
41	105·8	− 5	23
40·5	104·9	−10	14
40	104·0	−15	+5
39·5	103·1	−20	−4
39	102·2	0·54° =	1°
38·5	101·3	1 =	1·8
38	100·4	2 =	3·6
37·5	99·5	2·5 =	4·5

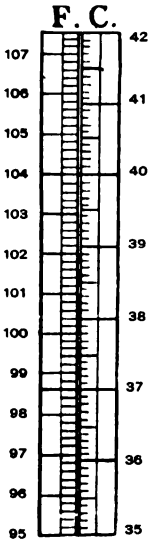


Fig. 404.

Fahrenheit and Centigrade scales compared.

Relation of the Metric to the Imperial Standard

Standards of mass.

1 milligramme	=	0·015 grain approximately.
1 centigramme	=	0·154 ,, ,,
1 decigramme	=	1·543 grains ,,
1 gramme	=	15·432 ,, ,,
1 kilogramme	=	35 oz., 120 gr., or 15,432 gr.

Standards of capacity.

1 cubic centimetre	=	17 minims approximately.
1 litre	=	35 fl. oz. 1 fl. dr. 34 min. approx.

Standards of length.

1 micron (μ)	=	0·001 millimetre or 0·00039 inch.
1 millimetre	=	0·039 inch.
1 centimetre	=	0·393 ,,
1 decimetre	=	3·937 inches.
1 metre	=	39·37 ,, nearly.

Digitized by Google

Relation of the Imperial to the Metric Standard

Standards of mass.

1 grain	=	0·064 gramme approximately.
1 ounce	=	28·349 grammes ,,
1 pound	=	453·592 ,, ,,

Standards of capacity.

1 minim	=	0·059 cubic centimetre approx.
1 fl. drachm	=	3·552 ,, centimetres ,,
1 fl. oz.	=	28·417 ,, ,, ,,
1 pint	=	568·336 ,, ,, ,,
1 gallon	=	4·545 litres.

Standards of length.

1 inch	=	2·54 centimetres.
1 foot	=	30·48 ,,
1 yard	=	91·44 ,,

Weights and Measures of the Metric System

Measures of mass.

1 milligramme = the thousandth part of one gramme, or 0·001 grm.
1 centigramme = the hundredth part of one gramme, or 0·01 grm.
1 decigramme = the tenth part of one gramme, or 0·1 grm.
1 gramme = weight of one millilitre of distilled water at 4° C. (39·2° F.), 1·0 grm.
1 dekagramme = 10 grammes, or 10·0 grm.
1 hectogramme = 100 grammes, or 100·0 grm.
1 kilogramme = 1,000 grammes, or 1,000·0 grm.

Measures of capacity.

1 millilitre or 1 cubic centimetre = the volume of one gramme of water at 4° C.
1 centilitre = the volume of 10 grammes of water at 4° C.
1 decilitre = the volume of 100 grammes of water at 4° C.
1 litre = the volume of 1,000 grammes (1 kg.) at 4° C.

Measures of length.

1 millimetre = one thousandth part of one metre, or 0·001 metre.
1 centimetre = one hundredth part of one metre, or 0·01 metre.
1 decimetre = one tenth part of one meter, or 0·1 metre.
1 metre = 1·0 metre.

Weights and Measures of the Imperial System

Measures of mass.

1 grain	gr.		
1 ounce (avoir.)	oz.	=	437·5 grammes.
1 pound	lb.	=	16 oz. = 7,000 grammes.

Measures of capacity.

1 minim	min.		
1 fluid drachm	fl. dr.	=	60 minims.
1 fluid ounce	fl. oz.	=	8 fluid drachms.
1 pint	O	=	20 fluid ounces.
1 gallon	C	=	8 pints.

Digitized by Google

Measures of length.

1 inch	in.		
1 foot	ft.	=	12 inches.
1 yard	yd.	=	36 inches.

Relation of Volume to Mass

1 minim is the volume at 62° F. of 0·911 grain of water.
1 fluid drachm is the volume at 62° F. of 54·687 grains of water.
1 fluid ounce is the volume of 1 ounce, or 437·5 grains of water.
1 pint is the volume of 1·25 pounds, or 8,750 grains of water.
1 gallon is the volume of 10 pounds, or 70,000 grains of water.
110 minims nearly = the volume at 62° F. of 100 grains of water.

Digitized by Google

Digitized by Google

INDEX

A

Abramis vimba, 792
Abscess of brain, amœbic, 466
—— of liver (*see* Liver abscess)
Acanthobdella, 852
Acanthocephala, characters of, 850
Acanthocheilonema perstans, 841
—— —— characters of, 842
—— —— embryo of, 842
—— —— geographical distribution of, 841
—— —— life-history and pathogenesis of, 843
Acanthophis antarcticus, 684
Acarina, 186, 853
Acarine dermatomycosis, 728
Acarus balatus, 856
—— scabiei, 854
Accès pernicieux, 43
Acids, fatty, in fæces, 904
Ackee poisoning, 681
Acocanthera, 679
Aconita ferox, 680
Acrocephalus orientalis, 243
Acropathia mutilante, 739
Actinic-ray-proof clothing, 325
Actinomycotic mycetoma, 709
Adenitis, non-venereal, 740
Adenium, 679
—— bœhmianum, 679
Adynamic remittent fever, 43
Æstivo-autumnal malaria parasite (*see* Subtertian malarial parasite)
Agar, glucose, preparation of, 891
—— glycerin, preparation of, 891
—— nutrient, preparation of, 890
Agave americana, 682
Agglomeration of trypanosomes, 116
Agglutination, 897
—— in bacillary dysentery, 409
—— in cholera, 386, 396
—— in enteric and enteric-like fevers, 303
—— —— —— —— technique of, 897
—— in infectious jaundice, 215
—— in typhus fever, 250
—— in undulant fever, 286, 902
—— in yellow fever, 204
—— macroscopic, 897
—— —— rapid method of, 898
Aglypha, 873
Ague, atypical 32
—— fit, 28
—— —— cold stage of, 29
—— —— duration of, 30
—— —— hot stage of, 29
—— —— premonitory stage of, 29
—— —— relation of, to stages of parasite, 33
—— —— spleen in, 31
—— —— sweating stage of, 29
Ague fit, types of, 32
—— —— urine in, 30
—— (*see also* Malarial fever)
Ainhum, 744
Aino, 761
Akamushi, 242
Aker lampong, 679
Akis spinosa, 814
Alcohol poisoning, 682
Alpine scurvy, 371
Amblyomma, 858
Amblyopia, malarial, 44
—— —— diagnosed from quinine amblyopia, 45
Ambulatory cholera, 391
American trypanosomiasis (*see* Trypanosomiasis, T. cruzi)
Amœba limax, 755
Amœbæ, intestinal, commoner differential characters of, 753
Amœbiasis (*see* Dysentery, amœbic)
Amphistomata, 786
Amphistomum conicum, 804
—— hominis, 804
—— watsoni, 803
Anæmia, endemic (*see* Ankylostomiasis)
Anákhré, 741
Anaplasma, 780
—— centrale, 780
—— marginale, 780
Anchylostoma (*see* Ankylostoma)
Anchylostomum americanum (*see* Necator americanus)
Ancistrodon contortrix, 684
—— piscivorus, 684
Angiostomidæ, characters of, 821
Anguillula intestinalis, 847
—— stercoralis, 847
Aniline gentian-violet stain, 929
Animal parasites and associated diseases, 553
Ankylostoma, 735
—— braziliense, 829
—— ceylanicum, 829
—— duodenale, 661, 829
—— —— description of, 661
—— —— dysenteric symptoms due to, 469
—— —— embryos of, 662
—— —— geographical distribution of, 660
—— —— ova of, in fæces, 655, 668 (footnote)
—— —— reproduction and mode of infection of, 662
Ankylostome dermatitis, 675
Ankylostomiasis, 658
—— campaign against, in United States, 675
—— convalescence in, 673
—— definition of, 658
—— geographical distribution of, 660
—— history of, 659

Digitized by Google

Ankylostomiasis, immunity from, 668
—— modes of infection with, 663
—— morbid anatomy and pathology of, 669
—— nomenclature of, 659
—— parasites of, 661
—— prophylaxis of, 673
—— Rockefeller Commission and, 672, 673, 675
—— symptoms of, 665
—— treatment of, 670
Annelida, characters of, 851
Anopheles bancrofti, 95 (footnote)
—— generic characters of, 92
—— ludlowi, 95 (footnote)
—— maculipennis, 12, 95, 843
Anophelini, characters of, 91
—— subgenera of, 94
Anoplura, 867
Antiarin, 679
Antiaris toxicaria, 679
Anticipating fevers, malarial, 32
Anti-hookworm campaign, 675
Antimony in dracontiasis, 646
—— in kala-azar, 157
—— in leishmaniasis Americana, 168
—— in oriental sore, 165
—— in schistosomiasis, intestinal, 574
—— —— of the Far East, 580
—— —— urinary, 566
—— in trypanosomiasis, 130
—— in ulcerating granuloma, 552
Anti-scorbutic vitamine, 352
Anti-typhoid inoculation, 307
Antivenene, 688
Aphthæ tropicæ, 473
Apocynaceæ, 680
Appendicostomy in bacillary dysentery, 427
Arachnida, 690, 853
Araneæ, 691
Araneida, 862
Archibald's stain for plague, 929
Arctomys bobac, 259
Areca catechu, 683
Argas, 858
—— miniatus, 187, 188
—— persicus, 174 (footnote), 187, 188
Argasidæ, 187
Arhynchobdella, 852
Aristoquinine in malaria 69
Arrow poisons, 679
Arrow-poisoned wounds, treatment of, 680
Arseno-benzol (*see* Salvarsan compounds)
Arthropoda, characters of, 852
—— classes of, 853
Ascariasis, 657
—— symptoms of, 657
—— treatment of, 658
Ascaridæ, characters of, 821
Ascaris, 469
—— lumbricoides, 657, 821
—— —— characters of, 821
—— —— geographical distribution of, 821
—— —— life-history of, 822
—— —— ova of, in fæces, 654
—— trichiura, 832
Asclepias, juice of, 680
Asopia farinalis, 814
Aspergillus, and mycetoma, 708
—— bouffardi, 710
—— fumigatus, 368
—— in pinta, 723
—— nidulans, 709, 710
—— niger, 368
Aspergillus pictor, 723
Astacus japonicus, 795
Asturian leprosy, 364
—— rose, 364
Asylum beriberi, 348
Athene noctua, 759, 778
Atoxyl in kala-azar, 157
—— in pellagra, 375
—— in relapsing fever, 185
—— in trypanosomiasis, 130, 137
Atriplex littoralis, 681
Atriplicism, 681
Atropine, 680
—— test, Marrie's, 303
Atypical agues, 32
Auchmeromyia luteola, 732, 733
Austen's classification of Glossinæ, table following p. 146

B

Babesia, and dengue, 222
—— bigemina, 187
—— bovis, 187, 779
—— canis, 187
—— ovis, 187
Bacillus aertrycke, infection with, simulating dysentery, 472
—— —— (suipestifer) fever, 311
—— coli infections, 312
—— dysenteriæ, 407
—— —— and allied organisms, cultural characters of, 408
—— —— Flexner-Y, 405, 408
—— —— isolation of, during life, 418
—— —— —— post mortem, 420
—— —— Shiga, 407
—— —— —— and allied bacilli, morphological and cultural characters of, 408
—— —— —— cultures of, 407
—— enteritidis fever, 311
—— fæcalis alkaligenes septicæmia, 311
—— gaertner, infection with, simulating dysentery, 472
—— lepræ, and tubercle bacillus, analogy between, 504
—— —— —— —— distinction between, 507
—— —— characters of, 506
—— —— culture experiments, failure of, 508
—— —— discovery of, 502
—— —— experimental inoculation with, 504
—— —— staining of, 506
—— mucosus capsulatus, 548
—— of cholera (*see* Comma bacillus)
—— paratyphosus-A, -B, -C, 294, 295, 296
—— pestis 253
—— —— characters of, 254
—— —— culture of, 254
—— —— discovery of, 253
—— —— modifications of virulence of, 255
—— proteus (X 19), 249
—— typhosus, 294, 295
Bacterial dysentery (*see* Dysentery, bacillary)
Bael fruit, in sprue, 486
Bagdad boil, 160
Balantidium coli, 466, 782
—— dysentery, 466
Baleri, 763
Balfour's infective granule, 173
Banti's disease (*see* Egyptian splenomegaly)

Digitized by Google

Barbeiro, 142, 869
Barbiers, 338
Barcoo rot (*see* Veld sore)
Barringtonia speciosa, 680
Bartonella bacilliformis, 542, 781
Basophiles, 886
Batran fever, 241
Becho, el, 429
Bed bugs, 868
Benzidin test for blood in fæces, 903
Beriberi, 338
— age and, 346
— asylum, 348
— cardiac attacks in, 346
— classification of, 346
— climatic conditions and, 347
— definition of, 338
— diagnosis of, 356
— —— erroneous, 344
— dropsical cases of, 342
— etiology of, 346
— food-deficiency theory of, 348
— geographical distribution of, 338
— heart and circulation in, 341
— history in, personal, 345
— — — of, 338
— hydrops, 346
— mixed paraplegic and dropsical cases of, 343
— modes of death in, 354
— morbid anatomy of, 353
— mortality of, 356
— nomenclature of, 346
— occupation and, 347
— overcrowding and, 347
— paraplegic cases of, 339
— pathology of, 353
— polyneuritis of fowls and, 349
— prognosis of, 355
— progress of cases in, 345
— prophylaxis of, 358
— sex and, 346
— ship, 347
— symptoms of, 339
— treatment of, 357
— uncertain course of, 345
— vitamines and, 351
Betel, 683
Bhang, 683
" Bicho Colorado," 856
Big heel, 746
Bile pigment in fæces, detection of, 903
— -salt medium for blood-cultures, preparation of, 893
Bilharzia hæmatobia (*see* Schistosoma hæmatobium)
— mansoni (*see* Schistosoma mansoni)
Bilharzial dysentery, 468
Bilharziasis (*see* Schistosomiasis)
Biliary cirrhosis, infantile, 496
Bilious remittent fever, diagnosis of, from yellow fever, 64
—— —— malaria, 42
—— typhoid of Griesinger (*see* Relapsing fever)
Bitis arietans, 684
— nasicornis, 860
Biuret reaction with trypsinized media, 893
Black fever, 235
—— sickness (*see* Kala-azar)
— snake, 684
— spores, 58
—— vomit in yellow fever, 200
Blackwater fever, 96
— —— definition of, 96
— — —— diagnosis of, 106
— —— distribution of, geographical, 96
Blackwater fever, distribution of, topographical, 97
— — —— epidemiology of, 98
— —— etiology of, 98, 100
— — — incubation period of, 104
— — — length of residence and, 99
— —— malaria theory of, 100
— —— mortality of, 106
— —— post-mortem appearances in, 106
— —— predisposing causes of, 98
— —— prophylaxis of, 109
— — —— quinine theory of, 102
— —— seasonal prevalence of, 98
— —— specific theory of, 102
— —— symptoms of, 104
— —— treatment of, 107
— —— urine in, 105
Blanfordia nosophore, 576
Blaps macronata, 851
Blastocystis hominis, 470
Blastomycosis, 713
—— pathological anatomy of, 715
—— treatment of, 715
Blighia sapida, 682
Blindworm snake, 873
Blood-cells, normal and abnormal, significance of, 885
— red, enumeration of, by Bürker counting apparatus, 888
— — — —— by Thoma-Zeiss hæmocytometer, 887
— — — polychromatic degeneration of, 886
— white, enumeration of, by Bürker counting apparatus, 888
— —— —— by Thoma-Zeiss hæmocytometer, 887
Blood-culture for enteric organisms, etc., technique of, 895
Blood-films, fluid, 881
—— for differential count of cells, staining of, 881
—— for protozoa, staining of, 881
—— malarial, staining of, 25
—— thick, preparation of, 879
—— thin, preparation of, 878
Blood-platelets, 886
Blue disease, 235
Bodo, 755
Boilidæ, 873
Boils, 701
—— treatment of, 702
" Bolus alba," 400
Boophilus, 858
Borax methylene-blue stain, 929
Bordet-Gengou test, 650
Borrel's blue, preparation of, 882
" Bosch yaws," 160
Bothriocephalus cristatus, 815
—— latissimus, 815
—— latus, 815
—— liguloides, 817
—— mansoni, 817
Boubas, 526
Bouffard's black mycetoma, 710
— white mycetoma, 711
Bouton d'orient, 160
" Brassy bodies," 39
Breakbone fever, 221
Bright's disease, malaria and, 55
Brill's disease, 249
" Broad tapeworm," 815
Bronchial spirochætosis, 189
Bruce's classification of pathogenic African trypanosomes, 758
Brumpt's white mycetoma, 711
Bubas Braziliana, 166

Digitized by Google

Bubonic plague, 267
—— —— mortality of, 269
Buccopharyngeal distomatosis, 788
Buffalo, 761
Bugs, 868
—— destruction of, 869
Bullinus contortus, 557, 800, 803
—— dybowski, 557, 800
—— forskali, 800
—— innesi, 557
Bungarus cæruleus, 684, 686
—— fasciatus, 684, 688
Burdwan fever, 147
Bürker counting apparatus, 888
Burri's indian-ink method, 912
Bushbuck, 761, 763
Buthus martensi, 690
—— maurus, 690
Bythinia striatula var. japonica, 790

C

Cæcostomy in bacillary dysentery, 428
Cænogonimus heterophyes, 792
Calabar swellings, 636
Calliphora vomitoria, 678 (figure)
Calymmato-bacterium granulomatis, 548
Cancaco, 659
Canis familiaris, 792
—— niloticus, 792
Cannabis indica, 682
Capybara, 762
Caraate, 720
Carapata disease, 170
Carassius auratus, 790
Caribi, 429
Carriers of bacillary dysentery, 416
—— of Entamœba histolytica, 435
—— of enteric fever, 293
—— —— —— detection of, 302
Carrion's disease, 541
Cassia alata, 717, 720
Castellani, and discovery of parasite of sleeping sickness, 112
Casts in urine, 909
Catoblepas gnu, 761
Caucus rhombeatus, 684
"Cellia," 94
Centigrade and Fahrenheit scales, relation between, 931
Centipedes, 872
—— bites of, 692
Centrurus, 690
Cerastes cornutus, 684
Ceratophyllus, 870
—— acutus, 259
—— fasciatus, 260, 760, 814
Cerbera odollam, 680
Cercaria stage of Schistosoma hæmatobium, 557
Cercariæ, 785
—— and fresh-water snails, 801
—— classification of, 801
Cercopithecus albigularis, 860
—— pousarguei, 860
Cerebral capillaries, embolism of, in malaria, 44
—— forms of subtertian malaria, 43
Cerebro-spinal fluid, examination of, 893
—— fever, rash of, 335
Cestodes, 676, 784, 804
—— characters of, 804
—— life-history of, 805
—— ova of, 655
—— parasitic in man, classification of, 806
Cestodes, treatment of affections due to, 677
Ceylon sore mouth, 473
Chætopelma olivacea, 692
Chagas' disease (*see* Trypanosomiasis, T. cruzi)
Chaparro in amœbic dysentery, 445
Chappa, 739
Charcot-Leyden crystals in fæces, 905
Chaulmoogra oil in leprosy, 522
Cheese-mites, 855
Cheiracanthus siamensis 846
Chiatopsylla, 870
Chigger, 725, 869
Chilomastix in bacillary-dysentery exudate, 417
—— mesnili, 470, 769
Chilopoda, 692, 872
Chlamydozoa, 782
Cholera, 380
—— agglutination in, 396
—— algid stage of, 390
—— ambulatory, 391
—— carriers, 395
—— definition of, 380
—— diagnosis of, 393
—— —— bacteriological, 394
—— —— —— rapid method of, 395
—— dysentery and, 472
—— epidemiology of, 380
—— etiology of, 381
—— geographical distribution of, 380
—— germ of (*see* Comma bacillus)
—— history of, 380
—— hyperpyrexia in, 391
—— immunity from, 388
—— incubation period of, 398
—— inoculation against, 398
—— isolation of organisms post mortem in, 903
—— local conditions favouring, 382
—— lower animals and, 388
—— morbid anatomy of, 392
—— mortality of, 396
—— pathology of, 392
—— precautions in, 403
—— "premonitory diarrhœa" and, 389
—— prophylaxis of, personal, 399
—— quarantine prevention of, 396
—— reaction stage of, 390
—— sequelæ of, 392
—— sicca, 391
—— symptoms of, 389
—— treatment of, 400
—— —— Cox's, 402
—— —— Rogers's, 400
—— typhoid, 390
—— water-borne, 382
Choleraic dysentery, 413
—— form of subtertian malaria, 45
Cholerine, 391
Chrysomyia macellaria, 729
Chrysops dimidiata, 633, 841
—— excutiens, 838
—— longicornis, 633, 865 (Fig. 363)
—— silacea, 633, 841
Chvostek's sign, 372
Chylous diarrhœa, 629
—— dropsy, 628
Chyluria, 613
—— causes of, 615
—— pathology of, 613
—— symptoms of, 614
—— treatment of, 615
Ciliophora, 749, 782
Cimex boueti, 139, 868
—— hemipterus (rotundatus), 766, 868
—— lectularius, 139, 174, 868

Digitized by Google

Cimicidæ, 868
Cirrhosis, infantile biliary, 496
Citellus beechyi, 259
—— columbianus, 238
Cladococlium hepaticum, 786
Cladorchis watsoni, 803
Climatic bubo, 740
Clonorchiasis, 651
—— diagnosis of, 652
—— geographical distribution of, 651
—— pathogenesis of, 651
—— prophylaxis of, 652
—— treatment of, 652
Clonorchis endemicus, 790
—— sinensis, 651, 790
—— —— geographical distribution of, 790
—— —— history of, 790
—— —— ova of, in fæces, 655 (Fig. 181)
—— —— pathogenicity of, 651
Clou de Gafsa, 160
Cnidosporidia, 781
Cobras, 684
Coccidia, 771
Coccidiosis, human, 772
Cœnurus glomeratus, 811
Coko, 526
Cole and Onslow's trypsinized casein, 891
Colitis, ulcerative, 471
Colubridæ, 873
Colubrine snakes, 686
Coma in malaria, 44
Comma bacillus, 384
—— —— causal relation of, to cholera, 386
—— —— cultivation of, 385
—— —— toxins of, 388
Complement-deviation in blastomyces, 715
—— in melitensis cases of undulant fever, 287
—— in paragonimiasis, 650
—— in schistosomiasis, intestinal, 573
—— —— of the Far East, 580
—— —— urinary, 565
—— in sprue, 474
—— in trypanosomiasis, 129
—— in typhus fever, 250
—— in yellow fever, 204
Congo floor maggot, 733
Conorhinus infestans, 141
—— megistus, 112, 138, 142, 757, 764, 869
—— protractus, 142
Constipation, post-dysenteric, treatment of, 428
Continued fever, malarial, 33
Copperhead snake, 684
"Copra itch," 855
Coral snake, 684
Cordylobia anthropophaga, 732
Corethrinæ, 90
Cotylogonimus heterophyes, 792
Cover-slips, cleaning of, 878
Cox's treatment of cholera, 402
Crab louse, 867
Craigia hominis, 770
Craw-craw, 738
Creeping eruption, 735
Crendiropoulo's medium, 893
"Crescent bodies," 6, 39
Cristispira, 783
—— balbianii, 783
Crithidia, 765, 766
Crotalinæ, 684, 874
—— synopsis of, 877
Crotalus, bites of, 687
—— durissus, 684
Crotalus horridus, 684
—— scutulatus, 684
—— terrificus, 684
Crustacea, 853
Cryptococcus capsulatus, 157, 714
—— farciminosus, 714, 767
—— linguæpilosæ, 714
Ctenocephalus, 870
—— canis, 152, 261, 766, 815
—— serraticeps, 152
Ctenodactylus gondii, 778
Ctenophthalmus, 870
Ctenopsylla, 870
—— musculi, 260 (footnote)
Culex fatigans, and dengue, 222
—— —— and Filaria bancrofti, 586, 590 (footnote)
—— pipiens, 590 (footnote)
Culicidæ, 83
—— sub-families of, 90
Culicinæ, 90
—— tribes of, 91
Culicini, 91
Culicoides, 866 (Fig. 369)
Culture media, bile-salt, 893
—— —— Crendiropoulo's, 893
—— —— Dieudonné's blood-alkali-agar, 894
—— —— for spirochætes, 894
—— —— Löffler's blood-serum, 892
—— —— MacConkey's bile-salt and lactose agar, 891
—— —— meat extract, 890
—— —— N.N.N., 894
—— —— nutrient agar, 890
—— —— —— broth, 890
—— —— peptone water, 891
—— —— standardization of, 889
—— —— sugar, 891
—— —— Thomson's serum agar, 892
—— —— trypsin agar, 892
—— —— useful, preparation of, 888
Curare, 680
Cutaneous leishmaniasis, 160
Cyclops bicuspidatus, 846
—— leuckartii, 817
—— quadricornis, 640, 846
—— strenuus, 816, 846
—— viridis, 640, 846
Cysticercus cellulosæ, 808

D

Daboia, 684
—— russellii, 685
Dandy fever, 221
Danysz's bacillus, 274
Dark-ground illumination, technique of, 910
Datura, 680
Davainea asiatica, 815
—— formosana, 815
—— madagascariensis, 814
—— —— characters of, 814
—— —— history of, 814
—— —— life-history of, 815
—— —— pathogenesis of, 815
Death adder, 684
Delafield's hæmatoxylin stain, 929
Delhi boil, 160
Demodecidæ, 854, 856
Demodex folliculorum var. hominis, 856
Dengue, 221
—— complications of, 227
—— convalescence in, 227
—— definition of, 221

Digitized by Google

Dengue, desquamation in, 227
—— diagnosis of, 228
—— eruption in, 226
—— etiology of, 222
—— geographical distribution of, 221
—— incubation period of, 224
—— meteorological conditions and, 223
—— mode of spread of, 221
—— morbid anatomy of, 228
—— mortality of, 228
—— mosquito and, 223
—— rash of, 335
—— relapses in, 228
—— rheumatoid pains in, 224, 227
—— sequelæ of, 227
—— stage of invasion of, 224
—— —— of remission of, 225
—— symptoms of, 224
—— terminal fever and eruption of, 225
—— treatment of, 229
—— variability of epidemic type of, 228
Denisonia superba, 684
Dermacentor, 858
— occidentalis, 238 (footnote)
— reticulatus, 187, 238 (footnote)
— venustus, 187
—— —— and spotted fever of Rocky Mountains, 235, 238, 239
—— —— and tick paralysis, 239 (footnote)
—— —— and typhus fever, 246
Dermacentroxenus rickettsi, 238
Dermatitis, ankylostome, 675
—— linearis migrans, 735
—— noxialis, 730
Dermatobia cyaniventris, 731
—— noxialis, 730
Dermatomycosis, 728
Dermatophilidæ, 870
Dermatophilus penetrans, 725
Dermotagra, 364
Derrengadera (*see* Trypanosomiasis, T. cruzi)
Desert sore, 699
—— —— etiology of, 699
—— —— treatment of, 701
Desvoidea obturbans, and dengue, 223
Detritus in fæces, 904
Dhobie's itch, 715
—— —— diagnosis of, 716
—— —— etiology and nomenclature of, 715
—— —— prophylaxis of, 718
—— —— symptoms of, 716
—— —— treatment of, 717
Diagnosis of fevers in tropics (*see* Fevers in tropics, diagnosis of)
Diamphidia locusta, 679
Diaptomus gracilis, 816
Diarrhœa alba, 473
—— hill, 490
"—— premonitory," 389
Diazo reaction, 908
—— —— in enteric fever, 306
Dibothriocephalidæ, characters of, 806
Dibothriocephalus grandis, ova of, in fæces, 656
—— latus, 815
—— —— characters of, 815
—— —— geographical distribution of, 815
—— —— life-history and pathogenesis of, 816
—— —— ova of, in fæces, 656
—— mansoni, 817
—— —— ocular sparganosis and, 818
Dibothrium mansoni, 817
Dicrocœlium buski, 788
Dicrocœlium dendriticum, 792
—— —— characters of, 792
—— —— history of, 792
—— —— life-history of, 792
—— heterophyes, 792
—— lanceatum, 792
Diemenia textilis, 684
Dientamœba fragilis, 431, 754
Dieudonné's blood-alkali-agar, preparation of, 894
Dilution of serum, progressive, in agglutination test, 897
Diphtheritic dysentery, 410
Diplacanthus nanus, 811
Diplogonoporus grandis, 818
Diplopoda, 872
Diptera, 865
Dipylidium caninum, 815, 871
—— —— characters of, 815
—— —— geographical distribution of, 815
Dirofilaria immitis, 594
—— magalhaesi, 838
Discomyces bovis, 709
—— maduræ, 709
—— (Nocardia) tenuis, 724
Disease of the Landes, 364
Diseases of undetermined nature, general, 338
—— —— —— local, 738
Distoma buski, 788
— cerebrale, 794
— conjunctum, 790
— felineum, 791
— hepaticum, 786
— heterophyes, 792
— innocuum, 790
— japonicum, 790
— (?) macrostomum, 785
— pulmonale, 794
— rathouisi, 788
— ringeri, 647, 794
— sibericum, 791
— sinense, 790
— spathulatum, 790
— westermanni, 794
Distomata, 786
Distomum caviæ, 786
—— hæmatobium (*see* Schistosoma hæmatobium)
Dobell's modification of Lavaditi's method, 923
Dochmius duodenalis, 829
Dog, and kala-azar, 152
Dog-flea, and kala-azar, 152
Donné's pus test, 909
Double continued fever, 314
Dourine, 762
Dracontiasis (*see* Guinea-worm infection)
Dracunculus medinensis, 639, 844
—— —— biological peculiarities of, 643
—— —— characters of, 640, 844
—— —— development of, in intermediary host, 846
—— —— embryo of, 845
—— —— geographical distribution of, 639, 844
—— —— larvæ of, 640
—— —— mode of infestation with, 641
—— oculi, 839
Dreyer's drop method, 897
Dropsy, epidemic, 361
"Dry beriberi," 346
Dube, 526
Dum-dum fever, 147
"Durango," 690
"Dutch-wife," 694

Digitized by Google

" Dysenteric abscess," 449
—— form of malarial fever, 46
—— —— —— —— treatment of, 77
—— rheumatism, 414
—— subtertian malaria, 46
Dysenteries, differential diagnosis of, 469
—— types of, 404
Dysentery, amœbic, carriers of, 436
—— —— definition of, 430
—— —— diagnosis of, 440
—— —— epidemiology of, 430
—— —— etiology of, 430 (*see also* Entamœba histolytica)
—— —— geographical distribution of, 430
—— —— hepatitis in, treatment of, 445
—— —— incubation period of, 439
—— —— liver abscess and, 446, 454
—— —— pathology of, 437
—— —— prophylaxis of, 445
—— —— superimposed on bacillary dysentery, 440
—— —— symptoms of, 439
—— —— treatment of, 441
—— —— —— by chaparro, 445
—— —— —— by emetine, 442
—— —— —— by eusol irrigations, 444
—— —— —— by ipecacuanha, 441
—— —— —— by neo-salvarsan, 444
—— —— —— by simaruba bark, 445
—— —— (*see also* Liver abscess)
—— bacillary, 405
—— —— acute, 412
—— —— carriers of, 416
—— —— choleraic, 413
—— —— chronic, 414
—— —— —— treatment of, 426
—— —— —— —— by eusol irrigation, 427
—— —— —— —— by nitrate-of-silver injections, 426
—— —— —— —— by vaccine, 426
—— —— —— —— surgical, 427
—— —— collapse in, treatment of, 425
—— —— complications of, 414
—— —— contagion in, 406
—— —— definition of, 405
—— —— diagnosis of, 416
—— —— —— by examination of stools, 417
—— —— —— from amœbiasis, 421
—— —— —— serological, 420
—— —— —— sigmoidoscopic, 421
—— —— dust as medium of infection of, 407
—— —— epidemiology of, 405
—— —— etiology of, 407
—— —— flies as carriers of, 406
—— —— food and clothing in, 428
—— —— fulminating, 412
—— —— geographical distribution of, 405
—— —— germs of, 407
—— —— incubation period of, 411
—— —— mild or catarrhal forms of, 412
—— —— pathology of, 409
—— —— predisposing causes of, 414
—— —— prognosis of, 422
—— —— prophylaxis of, 429
—— —— —— by inoculation, 429
—— —— relapsing, 413
—— —— stools in, 411
—— —— symptoms of, 411
—— —— treatment of, 422
—— —— —— by serum, 424
—— —— water as medium of infection of, 406
—— balantidium, 466
Dysentery, bilharzial, 468
—— followed by sprue, 478
—— kala-azar, 471
—— malarial, 471
—— organisms in fæces in, cultivation of, 902
—— relation of liver abscess to, 446
—— verminous, 468

E

" East Coast fever," 779
Echinococcifer echinococcus, 809
Echinorhynchus gigas, 850
—— moniliformis, 851
Echinostomum ilocanum, 797
—— malayanum, 798
Echis carinatus, 684, 687
Eckujin, 679
Egyptian splenomegaly, 498
—— —— definition of, 498
—— —— diagnosis of, 500
—— —— endemiology and etiology of, 498
—— —— morbid anatomy and pathology of, 500
—— —— symptoms of, 498
—— —— treatment of, 500
Ehrlich's hæmatoxylin stain, 930
Eimeria, 772
—— oxyspora, 773
—— schubergi, 772
—— wenyoni, 773
Eimeriidea, 772
Elaphe climacophora, 817
Elapinæ, 874
—— African, synopsis of, 876
—— American, 876
—— Asiatic, synopsis of, 876
—— Australian, synopsis of, 876
—— synopsis of, 876
Elaps corallinus, 684
Elephantiasis, 617
—— a filarial disease, 603
—— græcorum (*see* Leprosy)
—— inflammation a necessary antecedent of, 604
—— of arms, 626
—— of legs, 619
—— —— treatment of, 620
—— —— —— Handley's operation, 620
—— —— —— Kondoleon's operation, 621
—— —— —— Lanz's operation, 621
—— of limited skin areas, 627
—— of scrotum, 621
—— —— anatomical characters of, 621
—— —— treatment of, 623
—— —— —— operative, 623
—— of vulva and mammæ, 626
—— pathology of, 603
—— recurring erysipelatoid attacks in, 618
—— sequence of events in, 604
—— swelling in, clinical characters of, 619
—— —— macroscopic anatomy of, 619
Elephantoid fever, 606
Eliomys quercinus, 812
Embadomonas intestinalis, 769
Emetine in amœbic dysentery, 442
—— in oriental sore, 166
—— in urinary schistosomiasis, 567
Emetine-bismuth-iodide, 443
Encystment in liver abscess, 449
Endemic funiculitis, 616
—— hæmaturia (*see* Schistosomiasis, urinary)

Digitized by Google

Endemic hæmoptysis (*see* Paragonimiasis)
—— hypertrophy of os calcis, 746
Endermophyton concentricum, 719
—— indicum, 719
Endolimax nana, 431, 753
Enhydrina valakadien, 685
Entamœba coli, 431, 750
—— —— cysts of, 751
—— —— in bacillary-dysentery exudate, 417
—— —— incidence of, 752
—— detection of, in stools, 432
—— dysenteriæ (*see* Entamœba histolytica)
—— gingivalis, 431, 752
—— histolytica, 431, 749
—— —— carriers of, 435
—— —— —— incidence of, 436
—— —— cysts of, 434
—— —— life-history of, 435
—— —— non-pathogenic species of, 431
—— tetragena (*see* Entamœba histolytica)
Entamœbæ, discovery of, 431
—— in liver abscess, 448
Enteric fever, 291
—— —— agglutination in, methods of, 897
—— —— —— significance of, 901
—— —— bacteriology and pathology of, 293
—— —— carriers of, 293
—— —— —— detection of, 302
—— —— cultivation of organisms from fæces in, 903
—— —— diagnosis of, bacteriological, 302
—— —— —— by Marris's atropine test, 303
—— —— —— clinical, 298
—— —— —— from malarial remittents, 310
—— —— —— from paratyphoid and other fevers, 306
—— —— —— rash of, 336
—— —— —— serological, 302
—— —— diazo reaction in, 306
—— —— epidemiology of, 295
—— —— etiology of, 293
—— —— incubation period of, 296
—— —— inoculation against, 307
—— —— low pulse-temperature ratio in, 300
—— —— onset of, 296
—— —— organisms of, 294
—— —— paratyphoid fevers and, 306
—— —— "period of expectation" in, 303
—— —— post-mortem appearances in, 295
—— —— —— bacteriology of, 295
—— —— preparation of vaccines for, 308
—— —— propagation of, 291
—— —— prophylaxis of, 307
—— —— pyrexia in, 299
—— —— rose spots in, 301
—— —— splenic enlargement in, 301
—— —— symptoms of, 296
—— —— toxæmia in, 300
—— —— treatment of, 309
—— —— —— by vaccine, 309
—— —— triple vaccine in, 291, 308
—— —— Widal reaction in, 303
Enteric-like fevers, 311
Entero-colitis, acute, sprue secondary to, 479
Eosinophiles, 886
Epidemic dropsy, 361
Epidemic dropsy, definition of, 361
—— —— etiology of, 361
—— —— geographical distribution of, 361
—— —— history of, 361
—— —— morbid anatomy of, 363
—— —— symptoms of, 362
—— —— treatment of, 363
—— dysentery (*see* Dysentery, bacillary)
—— gangrenous rectitis, 429
Epithelial cells in urine, 909
Epizootic lymphangitis of horses, parasite of, 767
Erinaceus æthiopicus, 860
Eriocheir japonicus, 795
—— sinensis, 795
Eruptions of fevers in tropics, diagnosis of, 335
Erythrasma, 717
Erythroblasts, 886
Erythrocytes, 886
Erythrophlæum guineense, 679
Espundia (*see* Leishmaniasis Americana)
Euchinine in malaria, 69
Eugregarines, 771
Euparyhium malayanum, 798
Euphorbia candelabrum, 679
Euquinine in malaria, 68
Euscorpius italicus, 690
Eusol solution, to make, 313
Eustrongylus gigas, 825
—— visceralis, 825
Evolution par fixation directe, 757
—— —— indirecte, 764
Exanthematous glandular fever, 241
Exudates, pathological, spectroscopic examination of, 909

F

Fæces, examination of, chemical, 903
—— —— for comma bacillus, 394
—— —— for ova of ankylostomes, 668 (footnote)
—— —— —— of intestinal parasites, 653
—— —— microscopical, 904
—— —— spectroscopic, 909
—— organisms from, cultivation of, 902
—— —— recognition of, by agglutination, 902
—— protozoa in, Schaudinn's method of staining, 906
Faget's law, 199
Fahrenheit and Centigrade scales, relation between, 931
Fairley's reaction, 565
Famine fever, 170
Fannia canicularis, 678, 865 (Fig. 360)
—— scalaris, 678
Fasciola gigantea, 787
—— hepatica, 786
—— —— characters of, 787
—— —— geographical distribution of, 787
—— —— history of, 786
—— —— ova of, in fæces, 653
—— —— pathogenesis of, 788
—— humani, 786
—— lanceolata, 792
Fasciolopsis buski, 788
—— —— characters of, 788
—— —— geographical distribution of, 788
—— —— history of, 788
—— —— ova of, in fæces, 653

Digitized by Google

Fasciolopsis buski, pathogenesis of, 789
—— —— varieties of, 789
—— fülleborni, 789
—— rathouisi, 789
Fats in fæces, 904
Fat-soluble A, 352
Fatty acids in fæces, 904
Febris recurrens (*see* Relapsing fever)
—— undulans (*see* Undulant fever)
Felis catus, 847
—— concolor, 847
—— domesticus, 792
—— tigris, 847
"Fer de lance," 684
Fever, non-malarial remittent, 314
—— of Cairo, unidentified, 314
—— simple continued, 219, 314
Fevers in tropics, diagnosis of, 327
—— —— —— dengue, 330
—— —— —— enteric, 331
—— —— —— enteric-like fevers, 332
—— —— —— filarial fever, 334
—— —— —— helminthic fevers, 333
—— —— —— kala-azar, 330
—— —— —— liver-abscess fever, 331
—— —— —— malaria, 327
—— —— —— Oroya fever, 333
—— —— —— phlebotomus fever, 330
—— —— —— relapsing fever, 329
—— —— —— seven-day fever, 330
—— —— —— trypanosomiasis, 329
—— —— —— typhus fever, 332
—— —— —— undulant fever, 331
—— —— —— Weil's disease, 330
—— —— —— yellow fever, 330
—— tropical, imperfectly differentiated, 314
Fibrin in sections, demonstration of, 923
Field-mouse, and seven-day fever, 220
Fiji, filariasis in, 598
Filaria apapillocephala, 838
—— bancrofti, 581, 835
—— —— characters of, 597, 836
—— —— cretification of, 598
—— —— demonstration of, in blood, 582
—— —— dimensions of, 844
—— —— discovery of, 581
—— —— female, 597
—— —— geographical distribution of, 582, 835
—— —— host of, definitive, 583
—— —— —— intermediary, 590
—— —— life-history of, 583
—— —— male, 597
—— —— transference of, to human host, 596
—— bourgi, 635, 839
—— conjunctivæ, 838
—— demarquayi, 838
—— (Diroflaria) immitis, 598
—— diurna, 839
—— equina, 634
—— inermis, 838
—— juncea, 838
—— labiato-papillosa, 634
—— loa, 839
—— medinensis, 844
—— nocturna, 581, 835
—— oculi, 839
—— —— humani, 838
—— ozzardi, 838
—— —— dimensions of, 844
—— palpebralis, 841
—— papillosa, 838
—— perstans, 841
—— —— dimensions of, 844
—— philippinensis, 589
—— sanguinis hominis, 835
Filaria subconjunctivalis, 839
—— volvulus, 843
—— wücheri, 835
—— (*see also* Microfilaria)
Filariæ, dimensions of, 844
—— metamorphosis of, in mosquito, 592
Filarial abscess, 606
—— diseases, enumeration of, 605
—— glandular enlargement, 611
—— hydrocele, 617
—— lymphuria, 615
—— non-periodicity, 589
—— orchitis, 616
—— periodicity, 585
—— synovitis, 617
Filariasis, 581
—— age- and sex-incidence of, 598
—— history of, 581
—— morbid anatomy and pathology of, 599
—— originating in injury of lymphatic systems, 599
—— parasites of, nomenclature of, 581
—— —— pathological importance of, 581
—— prophylaxis of, 630
—— treatment of, 629
—— varieties of, 605
Filariidæ, characters of, 821
Fishes, poisonous, 689
Fixation of intestines for paraffin sections, 921
—— of tissues for paraffin sections, 920
—— —— —— —— by formalin, 920
—— —— —— —— by mercuric chloride, 920
—— —— —— —— by Zenker's fluid, 920
"Flagella" of malaria parasite, 5
"Flagellar" and "aflagellar," use of, 756 (footnote)
"Flagellate diarrhœa," 470
Flagellated body in malaria, 5
—— —— —— method of staining of, 883
—— —— —— source of, 6
Flea, rat- (*see* Rat-flea)
Fleas, characters of, 869
—— disinfection and, 871
—— synopsis of, 870
Flema salada, 364
Flexner's bacillus, 405, 408
Flood fever (*see* Japanese river fever)
Fontana's staining method, 912
Food-deficiency theory of beriberi, 348
—— —— of pellagra, 369
Forest yaws, 166
Fowls, and beriberi, 349
Framboesia (*see* Yaws)
Fugitive lymphatic swellings, 617
Fungous skin diseases, 705
Funiculitis, endemic, 616
Furunculosis, 701
Fusuria vermicularis, 823

G

Gametes of malaria parasites, 19
Gametocytes of malaria parasites, 19
Ganga, 683
Gangosa, yaws and, 532
Gangrenous rectitis, epidemic, 429
Garrow's agglutinometer, 898
Gastric form of malarial fever, 45
Gastrodiscoides hominis, 804
—— —— characters of, 804
—— —— geographical distribution of, 804
—— —— history of, 804

Digitized by Google

Gastrodiscoides hominis, pathogenesis of, 804
—— —— treatment for, 804
Gastrodiscus ægyptiacus, 804
—— hominis, 804
Gastrophilus, 735
Gauducheau's stain, 882
Gee's cœliac diarrhœa, 475
Gentian-violet stain, aniline, 929
Giardia (Lamblia) intestinalis, 469, 770
Giemsa's staining methods, 912
—— —— —— for paraffin sections, 922
Gigantorhynchus gigas, 850
—— moniliformis, 851
Glandular enlargement, filarial, 611
—— —— in diagnosis of fevers in tropics, 337
"Globi" of leprosy, 509
Gloriosa superba, 680
Glossina austeni, table following p. 146
—— —— distribution of, 144
—— brevipalpis, 145, table following p. 146, 761
—— —— distribution of, 145
—— —— group, characters of, table following p. 146
—— caliginea, 145, table following p. 146
—— fusca, 144, 145, 146, 761
—— —— group, characters of, table following p. 146
—— fuscipleuris, table following p. 146
—— longipalpis, table following p. 146
—— —— development of trypanosomes in, 763, 764
—— —— distribution of, 144
—— longipennis, table following p. 146, 762
—— —— distribution of, 144
—— medicorum, table following p. 146
—— morsitans, 112, 121, 135, 136, table following p. 146, 759, 761, 763, 764
—— —— distribution of, 144, 145
—— —— group, characters of, table following p. 146
—— nigrofusca, table following p. 146
—— pallicera, table following p. 146
—— —— distribution of, 144
—— pallidipes, table following p. 146
—— —— distribution of, 144
—— —— habits of, 145, 146
—— palpalis, 112, 117, 118, 119, 121, 135, 145, table following p. 146, 757, 763, 764
—— —— distribution of, 144, 145
—— —— group, characters of, table following p. 146
—— severini, table following p. 146 (footnote)
—— tabaniformis, table following p. 146
—— tachinoides, 112, 121, 146, table following p. 146, 763, 764
—— —— distribution of, 144
—— ziemanni, table following p. 146
Glossinæ, 143
—— Austen's classification of, 144, table following p. 146
—— distribution of, 144
—— habits of, 145
—— Newstead's classification of, 144 (footnote)
—— reproduction of, 145
—— resting attitude of, 143
—— rôle of, in trypanosomiasis, 117
Glucose agar, preparation of, 891
Glycerin agar, preparation of, 891
Glycophagus, 728
Glyptocranium gasteracanthoides, 692
Gnathostomidæ, characters of, 821
Gnathostomum hispidium, 847
—— spinigerum, 846
—— —— characters of, 846
—— —— geographical distribution of, 846
—— —— history of, 846
—— —— life-history and pathogenesis of, 847
Gondi, 778
Gonococcus, detection of, 910
Gordiaciæ, 849
Goundou, 741
—— a possible sequel of yaws, 535
Gower's hæmoglobinometer, 888
Grahamella (*see* Bartonella bacilliformis)
"Grain itch," 728
Granule-shedding in trypanosomes, 114, 117
Granules, starch, in fæces, 904
Granuloma inguinale (*see* Ulcerating granuloma of pudenda)
—— venereum (*see* Ulcerating granuloma of pudenda)
Gregarines, 770
Gregarinida, 770
"Grocer's itch," 728, 855
"Gros nez," 741
Ground itch, 675
Ground-squirrel, 238
—— of California, and plague 259
—— of Caucasus, and plague, 259
Guinea-worm infection, 639
—— —— diagnosis of, 645
—— —— parasite of (*see* Dracunculus medinensis)
—— —— prophylaxis of, 646
—— —— treatment of, 645

H

Hæmadipsa, 852
—— zeylanica, 736, 852
Hæmaphysalis, 858
—— leachi, 187
Hæmatin, hæmozoin and, 51 (footnote)
Hæmatobia, 144, 760
Hæmatopinus spinulosus, 769
Hæmatopota, 143, 865 (Fig. 364)
Hæmatoxylin and eosin stain, 883
—— (Ehrlich's) stain, 930
Hæmaturia, endemic (*see* Schistosomiasis, urinary)
Hæmaturic fever (*see* Blackwater fever)
Hæmenteria, 852
Hæmocystidium simondi, 778
Hæmocystozoon braziliense, 767
Hæmoflagellata, 755
—— nomenclature of, 766
Hæmoglobin, estimation of, 888
Hæmoglobinæmia in malaria, 51
Hæmoglobinuria in malaria, 52
Hæmoglobinuric fever (*see* Blackwater fever)
Hæmogregarina canis, 774, 776
—— jaculi, 774
—— muris, 774, 775
—— stepanowi, 775
Hæmogregarinidæ, 772, 774
Hæmolytic anæmia, acute, 45
Hæmonchus contortus, 826
Hæmoproteus, 778
—— columbæ, 778
Hæmoptysis, endemic (*see* Paragonimiasis)

Digitized by Google

Hæmorrhagic form of subtertian malaria, 46
Hæmosporidia, 776
Hæmosoin, 3, 4
Haffkine's anti-cholera inoculations, 398
—— —— —— results of, in recent wars, 399
—— anti-plague inoculations, 274
Halteridium, 778
"Halsoun," 787, 788
Haplosporidia, 781
Harvest-bugs, 856
Hascheesch, 682
"Heat-apoplexy," malaria and, 43
Heat-exhaustion, 316
—— definition of, 316
—— etiology of, 316
—— symptoms of, 317
—— treatment of, 317
Heat-hyperpyrexia, 317
—— auto-intoxication in, 318
—— choleraic type of, 320
—— definition of, 317
—— diagnosis of, 321
—— etiology of, 318
—— gastric type of, 320
—— geographical distribution of, 317
—— morbid anatomy of, 320
—— mortality of, 320
—— nomenclature of, 317
—— symptoms of, 319
—— treatment of, 321
Heat-stroke, 316
—— prevention of, 324
Helcosoma tropicum, 160
Helix pomatia, 765
Helminthology, medical, 724
"Helminthoma elastica," 610
Heloderma horridum, 689
Hemiptera, 868
"Henpuye," 741
Hepatic abscess (*see* Liver abscess)
Hepatitis, amœbic, treatment of, 445
Herpetic eruptions in malarial cachexia, 54
Herpetomonas, 151, 765, 766, 852
Heterogony, 785
Heterophyes ægyptiaca, 792
—— heterophyes, 792
—— —— characters of, 792
—— —— dysenteric symptoms due to, 469
—— —— geographical distribution of, 792
—— —— history of, 792
—— —— zoological distribution of, 792
—— yokagawa, 793
Hill diarrhœa, 490
—— —— distribution of, 490
—— —— etiology and pathology of, 490
—— —— symptoms of, 491
—— —— treatment of, 491
Hinton, M. A. C., and plague rats, 276
Hippobosca maculata, 762, 866 (Fig. 370
—— of dogs and camels, 161
—— rufipes, 762
Hirudinea, characters of, 851
Hirudo, 852
Histoplasma capsulatum, 767
Histoplasmosis, 157
Histricopsylla, 870
Hoplopsyllus, 870
Horse leech, 736
Hotechis pseudechis, 684
Hovin fever, 241
Hyalomma, 858
Hydatid cysts, 809
Hydrocele, filarial, 616, 617
Hydrochærus capybara, 762
Hydrophinæ, 684, 874
—— synopsis of, 875
Hydroquinine in malaria, 69
Hymenolepis diminuta, 813
—— —— characters of, 813
—— —— geographical distribution of, 813
—— —— life-history of, 814
—— murina, 811
—— nana, 811
—— —— characters of, 812
—— —— development of, 812
—— —— distribution of, geographical, 812
—— —— —— zoological, 812
—— —— history of, 811
—— —— ova of, in fæces, 655
—— —— pathogenesis of, 813
Hyoscyamine, 680
Hyoscyamus fahezlez, 680
Hyperparasitism in malaria, 57
Hyperpyrexia, heat- (*see* Heat-hyperpyrexia)
—— in cholera, 391
—— in diagnosis of fevers in tropics, 334
—— in malaria, 43
—— —— treatment of, 75
Hypoderma, 735
Hypsobia (Blanfordia) nosophora, 577, 578

I

Icterus gravis (*see* Infectious jaundice)
Idus idus, 792
—— melanotis, 792
Imperfectly differentiated fevers of tropics, 314
Imperial and metric standards, relation between, 932
Indian hemp, 682
—— Plague Commission, 260
Indian-ink method, 912
Indiella mansoni, 711
—— reynieri, 711
—— somaliensis, 711
Infantile biliary cirrhosis, 496
—— —— —— pathology of, 497
—— —— —— symptoms of, 496
—— —— —— treatment of, 497
Infection theory of pellagra, 368
Infectious jaundice, 211
—— —— definition of, 211
—— —— diagnosis of, 215
—— —— etiology of, 211
—— —— geographical distribution of, 211
—— —— pathological anatomy of, 215
—— —— prophylaxis of, 216
—— —— symptoms of, 214
—— —— treatment of, 216
Infective granule of Balfour, 173
—— granulomatous diseases, 501
Inoculation, prophylactic, in cholera, 398
—— —— in dysentery, 429
—— —— in enteric fevers, 307
—— —— in plague, 274
—— —— in relapsing fever, 185
—— —— in yellow fever, 208
Insecta, characters of, 853, 863
Intestinal myiasis, 677
—— parasites (*see* Parasites, intestinal)
—— sand in fæces, 905
Intestines, fixation of, for paraffin sections, 921

Digitized by Google

Intoxication theory of pellagra, 367
Inversion phenomenon, 902
Iodamœba bütschlii, 431, 753
—— —— cysts of, 754
"Iodine" cysts, 753
Iodophilia, 885
Ipecacuanha in amœbic dysentery, 441
Ipoh, 679
Isolation of organisms post mortem, 903
Isospora hominis, 772
Istra, 425
Ixodes, 858
—— reduvius, 186, 780
—— ricinus, 239 (footnote)
Ixodidæ, 187, 854, 857, 858
Ixodinæ, 857, 858

J

Jaffé's test for indican in urine, 908
Japanese river fever, 241
—— —— —— definition of, 241
—— —— —— diagnosis of, 244
—— —— —— —— rash of, 336
—— —— —— distribution of, 241
—— —— —— etiology of, 241
—— —— —— history of, 241
—— —— —— intermediary host of virus of, 855
—— —— —— mortality of, 241
—— —— —— pathological anatomy of, 244
—— —— —— prophylaxis of, 245
—— —— —— symptoms of, 243
—— —— —— treatment of, 245
Jaundice in diagnosis of fevers in tropics, 336
Jensen's method of identifying gonococcus, 912
Jongck test in beriberi, 356
Juxta-articular nodulee, 743

K

"Kabure," 579
Kakke, 338
Kala-azar, 147
—— and oriental sore, 159
—— definition of, 147
—— diagnosis of, 156
—— dysentery, 471
—— epidemiology of, 149
—— etiology of, 150
—— geographical distribution of, 148
—— history of, 147
—— incubation period of, 154
—— mode of transmission of, 152
—— morbid anatomy of, 156
—— parasite of, 150
—— predisposing causes of, 153
—— prophylaxis of, 159
—— splenic puncture in, 156
—— symptoms of, 154
—— treatment of, 157
—— —— with antimony, 157
Kaladunkh, 147
Katathermometer, Leonard Hill's, 326
Katayama disease, 575, 576, 579
"Katipo," 691
Kawa, 683
Kedani mite, 242, 855
—— —— disease, 241
Kerandel's symptom, 122
King cobra, 684
Klebs-Löffler bacillus, and veld sore, 699
701
"Koch's bodies," 780
Kola tree, 683
Koodoo, 761
Krabbea grandis, 818
Kraits, 684, 686
Kwan's fluke, 789

L

Laboratory methods in tropical medicine, 878
Lachesis lanceolatus, 684
Lachnosterna arcuata, 851
Lagochilascaris major, 823
—— minor, 823
"Lamblia enteritis," 469
—— intestinalis, 770
Lamus (*see* Conorhinus)
Landes, disease of, 364
Lankesteria culicis, 771
Larva migrans, 735
Lathyrism, 681
Lathyrus sativus, 681
Latrodectus curacaviensis, 691
—— formidabilis, 863
—— geometricus, 691
—— hasselti, 691
—— mactans, 691, 863
—— scelio, 863
—— tredecimguttatus, 691
Laveran, and discovery of malaria parasite, 1
Laverania malariæ, 38, 776
Leeches as pests, 736
Leishman body, 147, 159
Leishmania, 147, 766
—— braziliensis, 167
—— donovani, 147, 150, 766
—— infantum, 149 (footnote), 766
—— parasites resembling, 767
—— tropica, 161, 766
Leishmaniasis, 147
—— Americana, 166
—— —— diagnosis of, 168
—— —— distribution of, 166
—— —— symptoms and etiology of, 167
—— —— treatment of, 168
—— dermal, 165
Leishman's stain, 881
Lelaps echidninus, 776
"Leper juice," 507
Leproma, 507, 508
Leprosy, 501
—— age and, 503
—— bacillus (*see* Bacillus lepræ)
—— climate and, 504
—— conditions of infection in, 505
—— contagiousness of, 505
—— definition of, 501
—— diagnosis of, 509
—— etiology of, 503
—— —— cured-fish theory of, 506
—— galloping, 511
—— geographical distribution of, 502
—— heredity and, 504
—— history of, 501
—— in rats, 508
—— leproma in, 508
—— modern knowledge of, rise of, 502
—— mixed, 521
—— nerve, 517
—— —— prognosis of, 511
—— nodular, 514
—— —— prognosis of, 511

Digitized by Google

Leprosy, occupation and, 503
—— pathological anatomy of, 508
—— prognosis of, 510
—— prophylaxis of, 524
—— segregation in, 525
—— sex and, 503
—— social and hygienic conditions and, 503
—— stages of, 511
—— —— incubation period, 512
—— —— primary exanthem, 513
—— —— —— infection, 512
—— —— prodromata, 512
—— —— sequelæ, 516
—— —— specific deposit, 514
—— symptoms of, 511
—— treatment of, 522
—— —— by chaulmoogra oil, 522
—— —— by nastin, 524
—— —— by operation, 524
—— —— by sodium gynocardate, 523
—— —— —— morrhuate, 523
—— —— by thyroidin, 524
—— —— by tuberculin, 524
—— —— hygienic, 522
—— uninoculability of, 504
—— vaccination and, 525
—— white, diagnosis of leprosy from, 510
Leptodera intestinalis, 847
—— stercoralis, 847
Leptomonas, 765, 766
Leptospira hebdomadalis, 219, 783
—— icterohæmorrhagiæ, 211, 783
—— —— cultivation of, 213
—— icteroides, 193, 213, 783
—— —— —— animal experiments with, 196
—— —— media for cultivation of, 193
—— —— —— mosquito intermediary agent of, 195
—— —— occurrence of, in blood, 195
—— morsus-muris, 217, 783
Leptus autumnalis, 855
Leucocytes, varieties of, 885
Leucocytosis, 885
Leucocytozoon, 779
Leucodermia, 695
—— diagnosis of leprosy from, 510
Leucogobis mayedæ, 790
Leucopenia, 885
Leucopodia güntheri, 790
Levaditi's method, 923
—— —— Dobell's modification of, 923
Levitation method in examination of fæces, 656, 668 (footnote)
Lice, 867
Lichen tropicus, 693
Ligula mansoni, 817
Limnæa amygdalum, 801
—— humilis, 787
—— minuta, 787
—— natalensis, 560 (footnote)
—— oahensis, 787
—— truncatula, 787
—— viator, 787
Limnatis, 852
—— nilotica, 736
Lingua nigra, 714
Linguatula armillata, 860
—— constricta, 860
—— serrata, 859
Linguatulidæ, characters of, 859
Lithia carmine stain, 930
Lithobius forficatus, 772
Liver abscess, 446
—— —— adhesions in, 448
—— —— amœbæ in, 448
—— —— area of dullness in, 453
Liver abscess, aspiration in, 459
—— —— climate and, 447
—— —— definition of, 446
—— —— diagnosis of, 457
—— —— —— from malaria, 458
—— —— discharging into serous cavity, treatment of, 465
—— —— —— through lung, treatment of, 464
—— —— drainage by aspiration in, 464
—— —— duration of, 455
—— —— encystment in, 449
—— —— etiology of, 446
—— —— —— predisposing conditions, 447
—— —— —— race, sex, and climate, 447
—— —— fever in, 451
—— —— geographical distribution of, 446
—— —— morbid anatomy of, 447
—— —— mortality of, 456
—— —— periodicity of fever in, 451, 458
—— —— pulmonary inflammation in, 448
—— —— pus in, characters of, 448
—— —— —— pyogenic organisms in, 448
—— —— relation of, to amœbic dysentery, 446, 454
—— —— rupture of, 455
—— —— —— into bowel, 456
—— —— —— into lung, 455
—— —— —— into pericardium, 456
—— —— —— into peritoneum, 456
—— —— —— into pleura, 456
—— —— —— into stomach, 456
—— —— —— through skin, 456
—— —— symptoms of, 449
—— —— —— incidence of, 455
—— —— terminations of, 455
—— —— treatment of, 459
—— —— —— by aspiration, 464
—— —— —— operative, 461
—— —— —— —— Manson's method, 461
—— —— —— —— prognosis in, 465
—— —— —— —— transperitoneal route, 461
—— —— —— —— transpleural route, 461
—— —— —— postoperative, 463
—— enlargement of, in kala-azar, 156
—— in malaria, 50
—— in malarial cachexia, 55
—— parasites of, 647
—— pus, characters of, 448, 456
—— tropical (*see* Tropical liver)
Lizards, poisonous, 689
Loa loa, 631, 839
—— —— Calabar swellings and, 636
—— —— characters of, 839
—— —— distribution of, geographical, 631, 839
—— —— —— zoological, 633
—— —— history of, 631
—— —— larva of, 632
—— —— life-history of, 633
—— —— pathogenesis of, 635
Local diseases of uncertain nature, 738
Löffler's blood-serum, preparation of, 892
—— methylene-blue stain, 928
Low fever, 314
Lugol's solution, 907, 913
Lustig's injections for plague, 275
Lycosa tarentula, 692
Lygosoma sundevalli, 689
Lymph scrotum, 611
Lymphangitis and elephantoid fever, 606

Digitized by Google

Lymphatic swellings, fugitive, 617
—— trunks, thickened, 610
—— varices, cutaneous and deeper, 610
—— varix, pathology of, 601
Lymphocytes, significance of, 885
Lymphuria, 613, 615
Lynchia maura, 778
Lyperosia, 144
—— irritans, 866 (Fig. 367)

M

MacConkey's bile-salt and lactose agar, preparation of, 891
"Machoira," 690
Macrogametes, 19
Macromerozoites, 775
Madura foot (*see* Mycetoma)
Madurella mycetomi, 710
—— tozeuri, 711
Main-en-griffe, 520
Maize theory of pellagra, 367, 370
Mal de caderas, 762
—— de la rosa, 364
—— du coït, 762
—— rosso, 364
Malaria, 1
—— acclimatization and, 60
—— acquired immunity and, 60
—— acute hæmolytic anæmia in, 45
—— æstivo-autumnal, 41
—— anti-relapse treatment of, 69
—— arsenic in, 76
—— bilious remittent, diagnosis of, from yellow fever, 64
—— —— —— treatment of, 75
—— blood in, 49
—— "brassy bodies" in, 39
—— cardiac degeneration in, 55
—— clinical phenomena of, 28
—— complement-deviation test in, 63
—— "crescent bodies" in blood in, 6, 39
—— definition of, 1
—— diagnosis of, 62
—— —— effect of quinine in, 62
—— —— from liver abscess, 63, 458
—— —— from other paroxysmal fevers, 64
—— —— from typhoid and paratyphoid fevers, 65
—— —— from yellow fever, 64
—— —— microscopical, bearing of quinine on, 25
—— —— of vacuoles in, 24
—— —— periodicity in, 63
—— double infection of red cells in, 10
—— dysenteric forms of, 46
—— —— —— treatment of, 77
—— endemiology and epidemiology of, 56
—— etiology of (*see* Malaria parasites *and* Malaria, mosquito and)
—— flagellated bodies in, 5
—— —— —— method of staining, 883
—— food and drink in, 77
—— hæmoglobin value of corpuscles in, 49
—— hæmoglobinæmia in, 50
—— hæmoglobinuria in, 52
—— hæmorrhagic form of, 46
—— histology of, 2
—— history of, 1
—— hyperparasitism in, 57
—— hyperpyrexia in, 75
—— immunity and, 60
Malaria infection, disturbance of soil and, 59
—— —— endemic and epidemic fluctuations of, 57
—— —— geographical range of, 56
—— —— influence of altitude in, 58
—— —— —— of atmospheric temperature in, 58
—— —— —— of latitude and season in, 56
—— —— —— of local conditions in, 56, 59
—— —— —— of meteorological conditions in, 60
—— —— —— of moisture in, 58
—— —— —— of winds in, 58
—— —— mixed, 33
—— —— time of day and, 59
—— leucocytes in, 49
—— liver in, 50
—— microscopical examination of blood in, 22
—— morbid anatomy of, 49
—— mosquito and, 10, 83
—— oligocythæmia in, 49
—— parasites as means of diagnosis, 24
—— —— benign, 27
—— —— changes in, in human cycle, 3
—— —— characters of, tabulated, 30
—— —— classification of, clinical, 27
—— —— complete cycles of, in man and birds, 19
—— —— "crescent bodies" of, 6, 39
—— —— cultivation of, 26
—— —— endogenous cycle of, 3, 19
—— —— exogenous cycle of, 5, 13, 19
—— —— extracorporeal cycle of, 5, 13, 19
—— —— "flagellated bodies" of, 5
—— —— —— —— formation of, 8
—— —— —— —— source of, 6
—— —— in mosquito, 5, 13, 19
—— —— —— encysted or zygote stage of, 15
—— —— —— sporozoite or infective stage of, 17
—— —— —— travelling vermicule stage of, 13
—— —— intracorporeal cycle of, 3, 19
—— —— latent phase of, 21
—— —— life-spans of, 3
—— —— malignant (*see* Malaria parasites, subtertian)
—— —— morphology of, 2
—— —— possibility of undiscovered phase of, 21
—— —— quartan, 33
—— —— structure of, in human cycle, 3
—— —— subtertian, 27, 38
—— —— —— "crescent bodies" of, 6, 39
—— —— tertian, 36
—— —— transference of, to human host, 18
—— pathognomonic signs of, 62
—— pathology of, 49
—— periodicity, cause of, 52
—— —— as diagnostic test, 63
—— pernicious attacks of, 43
—— —— algid, 45
—— —— —— pathology of, 47
—— —— —— treatment of, 76
—— —— cerebral, 43
—— phagocytosis in, 23
—— pigment in, 50
—— —— nature and source of, 50
—— —— yellow, 51
—— pigmented leucocytes, 23
—— polycholia in, 51

Digitized by Google

Malaria, proof of parasitic nature of, 2
—— prophylaxis of, 78
—— —— education in, 82
—— relapse in, influence of meteorological conditions on, 60
—— spleen in, 50, 54, 76
—— staining of blood in, 25
—— syncopal form of, 46
—— treatment of, 66
—— —— by drugs, other than quinine, 76
—— —— by quinine (*see* Quinine in treatment of malaria)
—— —— by Warburg's tincture, 74
—— —— prophylactic, 81
Malarial amblyopia, 44
—— blood, staining of, 25
—— cachexia, pathology of, 54
—— —— symptoms of, 53
—— —— treatment of, 76
—— coma, 44
—— dysentery, 471
—— fever, adynamic remittent, 43
—— —— algid, 45
—— —— —— treatment, 74, 76
—— —— bilious remittent, 42
—— —— —— —— treatment of, 75
—— —— cause of, 52
—— —— cerebral, 43
—— —— clinical forms of, 32
—— —— —— phenomena of, 28
—— —— differential diagnosis of, 48
—— —— embolism of cerebral capillaries in, 44
—— —— hyperpyrexia in, 43
—— —— malignant (*see* Malarial fever, subtertian)
—— —— quartan, 33
—— —— —— ague fit in, 36
—— —— —— geographical distribution of, 35
—— —— —— parasite of, 33
—— —— —— treatment of, 66
—— —— quotidian, 28
—— —— remittent types of, 42
—— —— —— diagnosis of enteric from, 310
—— —— subtertian, 38
—— —— —— algid forms of, 45
—— —— —— amblyopia in, 44
—— —— —— characters of, 39
—— —— —— choleraic, 45
—— —— —— clinical forms of, 42
—— —— —— complications of, 47
—— —— —— differential diagnosis of, 48
—— —— —— "double crisis" in, 40
—— —— —— dysenteric, 46
—— —— —— embolism of cerebral capillaries in, 44
—— —— —— gastric, 45
—— —— —— geographical distribution of, 41
—— —— —— hæmolytic anæmia in, acute, 45
—— —— —— hæmorrhagic, 46
—— —— —— hyperpyrexia in, 43
—— —— —— microscopical examinations in, 41
—— —— —— parasite of, 38
—— —— —— pernicious attacks in, 43
—— —— —— psychical disturbances in, permanent, 44
—— —— —— syncopal, 46
—— —— —— treatment of, 69
—— —— typhoid, remittent, 42
—— —— typical, 28
—— —— —— cold stage of, 29
Malarial fever, typical, duration of fit in, 30
—— —— —— hot stage of, 29
—— —— —— premonitory stage of, 29
—— —— —— sweating stage of, 29
—— hyperpyrexia, 43
—— —— treatment of, 75
—— invasion, circumstances favouring, 60
—— orchitis, 616
—— pigment, distribution of, 50
—— —— nature and source of, 50
—— —— yellow, 51
—— rashes, 47
—— theory of blackwater fever, 100
—— toxin, acquired tolerance of, 61
Malignant malarial fevers, 39
"Malmignatte," 691, 863
Malta fever (*see* Undulant fever)
"Mamanpian," 529
Margaropus, 858
—— annulatus, 187
—— australis, 187, 780
—— bovis, 187
—— decoloratus, 187
Marmot, and plague, 259
Marmota flaviventer, 238
Marris's atropine test, 303
Mass to volume, relation of, 933
Mastigophora, 749, 755
Maurer's dots, 886
Mayer's acid hæmalum stain, 922
—— hæmatoxylin stain, 930
Mbori, 760
Measles, rash of, 336
Measurement of microscopic objects, 884
Meat extract, preparation of, 890
Mediterranean fever (*see* Undulant fever)
—— yellow fever (*see* Infectious jaundice)
Megaloblasts, significance of, 886
Megalocytes, significance of, 886
Melania gottschei, 795
—— libertina, 790, 794, 795
—— obliquegranulosa, 795
—— paucicincta, 795
Melanuric fever, 96
Melolontha vulgaris, 850
Merozoites, 19
Mesogonimus heterophyes, 792
—— pulmonalis, 794
—— ringeri, 794
—— westermanni, 794
Metagonimus yokagawai, 793
—— —— characters of, 794
—— —— distribution and life-history of, 793
Methylene-blue stain, borax, 929
—— —— watery, 929
Metorchis conjunctus, 790
Metric and imperial standards, relation between, 931
—— system, weights and measures of, 932
Mianeh fever, 170, 180
Micrococcus melitensis, 279
—— —— cultures of, 280
—— paramelitensis, 279
Microcyte, significance of, 886
Microfilaria bancrofti, characters of, 583
—— —— demonstration of, in blood, 582
—— —— distribution of, when absent from peripheral circulation, 587
—— —— life of, in mosquito, 590
—— non-periodic strains of, 589
—— periodicity of, 585

Digitized by Google

Microfilaria demarquayi, 581
—— diurna, 581, 631, 632, 841
—— loa, 581
—— —— distinction of, from mf. bancrofti, 633
—— ozzardi, 581
—— perstans, 581, 842
—— volvulus, 639
Microfilariæ, enumeration of, 587, 588
—— films for demonstration of, 880
—— periodicity of, 585
—— retirement of, to larger arteries and lungs, 587
Microgametes, 748
Micromerozoites, 775
Microscopic objects, measurement of, 884
Microsporon furfur, 716
—— mansoni, 716
—— minutissimum, 716, 717
Microtrombidium molestiesimum, 856
—— wichmanni, 856
Microtus, 855
—— montebelli, and seven-day fever, 220
Midges, differentiation of, from mosquitoes, 90
"Miescher's tubes," 781
Milletia seriacea, 680
Millipedes, 872
Milvus parasiticus, 792
Miner's anæmia (*see* Ankylostomiasis)
Miracidium, 785
"Mixed beriberi," 346
Moccasin snake, 684
Mokkui fever, 241
Monilia psilosis, 474
Mononuclears, large hyaline, 886
Montoyella, 723
Mosquitoes, anatomy of, 87
—— and dengue, 222
—— and filariasis, 590
—— and malaria, 10, 83
—— and undulant fever, 281
—— and yellow fever, 195
—— caging of, 925
—— collecting of, 925
—— diagnosis of, from other blood-sucking insects, 89
—— dissection of, 925
—— geographical range of, 83
—— life-history of, 83, 84
—— migrations of, 87
—— mounting of, 926
—— sections of, celloidin, 927
—— —— paraffin, 928
—— species known to foster malaria parasite, 94
—— sub-families of, 90
—— transportation of, 927
Mosquito-malaria theory, 10
Mosquito-nets, 80
Mosquito-veils, 80
"Mother yaws," 529
Mozambique ulcer, 696
Mucor racemosus, 368
Mucus in fæces, 905
Mumu fever, 607
Muræna, 689
Murrina, 760
Mus minutus, 812
—— musculus, 812
Musca domestica, 865 (Fig. 359)
—— —— as carrier of dysenteric infection, 406
—— luteola, 733
Muscidæ, 144
Mycetoma, 705
Mycetoma, actinomycotic, 709
—— Bouffard's black, 710
—— —— white, 711
—— Brumpt's white, 711
—— Carter's black, 710
—— classification, etiology, and histology of, 708
—— definition of, 705
—— history and geographical distribution of, 705
—— morbid anatomy of, 712
—— Nicolle's white, 710
—— Reynier's white, 711
—— symptoms of, 705
—— treatment of, 713
—— Vincent's white, 709
Mygale, 692
Myiasis from Auchmeromyia luteola, 733
—— from Chrysomyia macellaria, 729
—— from Cordylobia anthropophaga, 732
—— from Dermatobia cyaniventris, 730
—— intestinal, 677
—— linearis, 735
Myriapoda, 692, 872
"Myzomyia," 94
"Myzorhynchus," 94

N

Nagana, 111, 134, 761
Naja bungarus, 684
—— flava, 684
—— haja, 684
—— tripudians, 684, 685
Naso-pharyngeal leishmaniasis, 166
Nastin in leprosy, 524
Necator americanus, 661, 829
—— —— characters of, 830
—— —— history and geographical distribution of, 829
—— —— life-history of, 830
Neisser's stain, 929
Nemathelminthes, 784, 819
Nematodes, 819
—— characters of, 819
—— life-history of, 820
—— ova of, in fæces, 654
—— parasitic in man, classification of, 821
Neopsylla, 870
Neo-salvarsan (*see* Salvarsan compounds)
Neosporidia, 781
Nerium odorum, 680
Newstead's classification of Glossina, 144 (footnote)
Nicolle, Novy, and Macneal (N.N.N.) medium, preparation of, 894
Nicolle's white mycetoma, 710
Nile boils, 701
Nocardia carougeaui, 743
Nodular dermatitis, 738
Noguchi's medium for cultivation of spirochætes, preparation of, 894
Non-malarial remittent fevers, 314
Nonne-Apelt test for globulin in cerebro-spinal fluid, 896
Normoblasts, 886
Notechis scutatus, 684, 685
Nutrient agar, preparation of, 890
—— broth, preparation of, 890
Nuttallia equi, 187, 780
—— herpestidis, 780
"Nyssorhynchus," 94

Digitized by Google

O

Obermeier, and discovery of Spironema recurrentis, 171
Ochromyia anthropophaga, 732
Octomitidæ, 770
Ocular sparganosis, 818
Odau-eki, 211
Œsophagostomum apiostomum, 827
—— —— in dysentery, 469
—— brumpti, 827
Œstridæ, 732, 735
Œstromyia, 735
Oleum gynocardium, 522
Oligocythæmia in malaria, 49
Omentopexy in treatment of Egyptian splenomegaly, 500
Onchocerca gibsoni, 637
—— volvulus, 637, 843
—— —— and craw-craw, 738
—— —— description of, 638, 843
—— —— eye lesions and, 639
—— —— geographical distribution of, 637
—— —— history of, 637
—— —— life-history of, 638
—— —— pathogenesis of, 638
Onchocerciasis, human, 637
Onyalai, 746
Oöcysts, 748
Oökinetes, 748
Ophidia, classification of, 872
Opisthoglypha, 874
Opisthorchis felineus, 790, 791
—— —— characters of, 791
—— —— history and geographical distribution of, 791
—— —— varieties of, 792
—— noverca, 790
—— —— characters of, 791
—— —— history of, 791
—— sinensis, 790
—— viverrini, 792
Opium poisoning, 682
Oppilatio, 659
Oriental sore, 160
—— —— age and, 162
—— —— and kala-azar, 159
—— —— definition of, 160
—— —— diagnosis of, 160
—— —— distribution of, 160
—— —— etiology of, 161
—— —— history of, 160
—— —— incubation period of, 162
—— —— methods of infection of, 161
—— —— occupation and, 162
—— —— race and, 162
—— —— sex and, 162
—— —— social conditions and, 162
—— —— symptoms of, 162
—— —— —— constitutional, 162
—— —— treatment of, 165
—— —— —— by antimony, 165
Ornithodoros, 858
—— moubata, 139, 174, 176, 177, 187, 843
—— savignyi, 174, 181, 187, 188
"Oro," 681
Oroya fever, 541
—— —— definition of, 541
—— —— etiology of, 541
—— —— geographical distribution of, 541
—— —— pathology of, 543
—— —— prophylaxis of, 544
—— —— symptoms of, 543
Ova of Ankylostoma duodenale, 655, 668 (footnote)
Ova of Ascaris lumbricoides, 654
—— of Clonorchis sinensis, 655 (Fig. 181), 790
—— of Davainea madagascariensis, 815
—— of Dibothriocephalus latus, 655 (Fig. 656), 656
—— of Dicrocœlium dendriticum, 792
—— of Diplogonoporus grandis, 656
—— of Fasciolopsis buski, 789
—— of Gastrodiscoides hominis, 804
—— of Heterophyes heterophyes, 655 (Fig. 181), 793
—— of Hymenolepis nana, 655, 812
—— of intestinal parasites, examination of fæces for, 653
—— —— —— impaction of, in human appendix, 656
—— —— —— method of concentrating, 656
—— —— —— —— of preserving, 656
—— of Metagonimus yokagawai, 794
—— of Necator americanus, 654 (Fig. 179)
—— of Opisthorchis noverca, 655 (Fig. 181), 791
—— of Oxyuris vermicularis, 653, 654 (Fig. 179)
—— of Paragonimus westermanni, 648
—— of Schistosoma hæmatobium, 555
—— —— in urine, 909
—— —— japonicum, 577
—— —— mansoni, 570, 571
—— of Strongyloides stercoralis, 654 (Fig. 179), 848
—— of Tænia saginata, 655
—— —— solium, 655
—— of Trichostrongylus instabilis, 654 (Fig. 179), 826
—— of Trichuris trichiura, 654
—— of Watsonius watsoni, 803
Oxydase reaction 886
Oxyuris vermicularis, 823
—— —— characters of, 823
—— —— life-history and pathogenesis of, 824
—— —— ova of, in fæces, 653

P

Pangonia rüppellii, 866 (Fig. 365)
Pani-ghao, 675
Papataci fever, 230
Paracholera, dysentery and, 472
Paraffin sections, cutting and mounting of, 921
—— —— demonstration of fibrin in, 923
—— —— —— of bacteria in, 923
—— —— fixation of, 920
—— —— method of using Giemsa stain for, 922
—— —— staining of, 922
Paragonimiasis, 647
—— diagnosis of, 650
—— geographical distribution of, 647
—— history of, 647
—— parasite of, 649
—— pathological anatomy of, 649
—— prophylaxis of, 650
—— symptoms of, 647
—— treatment of, 650
Paragonimus westermanni, 647, 794
—— —— characters of, 794
—— —— geographical distribution of, 794
—— —— life-history of, 795
—— —— pathogenesis of, 647

Digitized by Google

Paramœba hominis, 770
Paramphistomum cervi, 803
—— watsoni, 803
Parangi, 526
Parasaccharomyces ashfordi, 474
—— —— autolysate of, 488
Parasites, animal, and associated diseases, 553
—— intestinal, 653
—— —— ova of, examination of fæces for, 653
—— —— —— method of concentrating, 656
—— —— —— —— of preserving, 656
—— of circulatory system, 553
—— of liver, 647
—— of lung, 647
—— of lymphatic system and connective tissue, 581
—— of malaria (*see* Malaria parasites)
Paratyphoid-A fever, diagnosis of rash of, 336
Paratyphoid-B fever, 296
Paratyphoid fevers, diagnosis of enteric from, 306
Paropisthorchis caninus, 790
Patau, 242
Paullinia pinnata, 680
Pediculoides, 855
—— ventricosus, 728
Pediculus capitis and typhus fever, 246
—— corporis and typhus fever, 246
—— humanus, 174, 176, 867
—— —— capitis, 867
Pellagra, 364
—— age and, 365
—— definition of, 364
—— diagnosis of, 375
—— epidemiology of, 366
—— etiology of, 365
—— —— food-deficiency theory of, 369
—— —— infection theory of, 368
—— —— intoxication theory of, 367
—— —— maize theory of, 367, 370
—— geographical distribution of, 364
—— history of, 365
—— in British Isles, 364 (footnote)
—— morbid anatomy of, 374
—— occupation and, 365
—— season and, 366
—— sex and, 365
—— symptoms of, 371
—— treatment of, 375
—— typhus, 374
—— vitamines and, 369
Pellarina, 364
Pemphigus contagiosus, 703
—— —— treatment of, 704
—— leprosus, 517
Penicillium glaucum, 368
—— in pinta, 723
—— montoyai, 723
Pentastoma tæniodes, 859
Pentastomidæ, 859
Pentastomum constrictum, 860
Pentatrichomonas, 769
Peptone water, preparation of, 891
Periodicity, filarial, 585
—— malarial, 52
—— —— as diagnostic test, 63
Periplaneta americana, 815
—— orientalis, 815
Pernicious attacks in subtertian malaria, 43
Pestis siderans, 268
Pfeiffer's reaction, 389
Phagedæna, tropical sloughing, 696
Phlebotomus fever, 230
Phlebotomus fever, definition of, 230
—— —— diagnosis of, 233
—— —— distribution of, 230
—— —— etiology of, 230
—— —— history of, 230
—— —— pathology of, 232
—— —— prophylaxis of, 233
—— —— symptoms of, 232
—— —— treatment of, 233
—— genus, 231, 766
—— —— characters of, 233
—— papatasii, 231
—— possible carrier of Leishmania tropica, 161
Phoorsa, 684
Phthirus pubis, 867
Physaloptera caucasia, 832
—— mordens, 831
Physopsis africana, 560
Pian, 526
—— bois, 166
Pica, in ankylostomiasis, 666
Piedra, 723
Pigment, malarial, 3, 4
—— —— nature and source of, 50
Piles, internal, 471
Pinta, 720
—— definition of, 720
—— diagnosis of, 723
—— etiology of, 722
—— geographical distribution of, 720
—— symptoms of, 721
—— treatment of, 723
Piper betel, 683
Piroplasma, 779
—— bigeminum, 779
—— bovis, 780
—— caballi, 779
—— canis, 779, 780
—— mutans, 779, 780
Pityriasis versicolor, 716
Placobdella, 852
Plague, 252
—— age and, 265
—— atmospheric temperature and, 265
—— bubonic, 267
—— —— mortality of, 269
—— definition of, 252
—— diagnosis of, 270
—— distribution of, geographical, 252
—— —— seasonal, 262
—— epidemics of, 252
—— —— duration of, 265
—— —— extension of, 265
—— etiology of, 253
—— experimental, 255
—— feeding experiments in, 256
—— Haffkine's inoculations for, 274
—— history of, 252
—— in lower animals, 256
—— incubation period of, 265
—— inoculability of, 255
—— isolation of organisms post mortem in, 903
—— Lustig's injections for, 275
—— morbid anatomy and pathology of, 269
—— occupation and, 265
—— pneumonic, 269
—— —— mortality of, 269
—— predisposing causes of, 264
—— prophylaxis of, general, 271
—— —— personal, 274
—— quarantine in, 271
—— relapses in, 269
—— rôle of flea in, 260
—— —— of marmot and other rodents in, 259

Digitized by Google

Plague, rôle of rat in, 256
—— septicæmic, 268
—— serum-therapy in, 276
—— sex and, 265
—— susceptibility of lower animals to, 256
—— symptoms and stages of, 265
—— treatment of, 275
Planorbis boissyi, 557, 558, 565
—— centrimetralis, 800
—— exustus, 801
—— guadaloupensis, 800
—— marginatus, 792
—— olivaceus, 560
Plasmodium, characters of, 776
—— falciparum, 38, 776
—— kochi, 778 (figure)
—— life-cycle of, 776
—— malariæ, 33, 776
—— vivax, 36, 776
Platelets, blood-, 886
Platyhelminthes, 804
Plecoglossus altivelis, 794
Plerocercoides prolifer, 818
Plerocercus prolifer, 818
Plotosus anguillaris, 690
Pneumonic plague, 269
Poisonous fishes, 689
—— lizards, 689
Poisons, animal, 684
—— arrow, 679
—— used for criminal purposes, 680
—— vegetable, 679
Polka fever, 221
Pollenia, 153
Polycholia in malaria, 51
Polychromasia, 886
Polymastigina, 768
Polymorphonuclear, neutrophile, 885
Polyneuritis endemica, 338
—— gallinarum, 349
Ponos, 147
Porocephalus armillatus, 860
—— —— characters of, 860
—— —— discovery of, 860
—— —— distribution of, geographical, 860
—— —— —— zoological, 860
—— —— life-history of, 861
—— —— pathogenesis of, 861
—— moniliformis, 860
Postponing fevers, malarial, 32
Potamon dehaanii, 795
—— obtusipes, 795
"Premonitory diarrhœa," 389
Preserving mosquitoes, 925
—— tissues, 924
Prickly heat, 693
—— —— treatment of, 694
Principe, trypanosomiasis - prophylaxis in, 133
Progressive dilution of serum, in agglutination, 897
Protein value, biological, 370
Proteosoma grassii, 776
Proteroglypha, 874
Proteus vulgaris, 249
Protista, 748
Protomonadina, 755
Protopathic sprue, 478
Protozoa, characters of, 748
—— ciliate, 782
—— classification of, 748
—— culture of, technique of, 895
Protozoal dysentery (*see* Dysentery, amœbic)
Prowazekia, 755
Pseudactinomycosis, 705
Pseudalius trichina, 833
Pseudoleuksæmia infantum, 498
Pseudo-parasites in fæces, 905
Pseudorasbora parva, 790
Pseudo-typhus fever, 241
Psilosis, 473
—— linguæ, 473
—— pigmentosa, 364
Psychotria ipecacuanhæ, 442
Ptomaine poisoning, simulating dysentery, 472
Puff adder, 684
Pulex irritans, 815
—— —— and plague, 260 (footnote)
Pulicidæ, 870
Pulmonary abscess in liver abscess, 448
—— inflammation in liver abscess, 448
Pulque, 682
Pulses, as anti-scorbutics, preparation of, 378
Purru, 526
"Pyæmic abscess," 449
Pygiopsylla, 870
Pyogenic organisms, in liver abscess, 448
Pyosis Mansoni, 703
"Pyretophorus," 94
Pyrexia of unknown origin, 306, 314
Pyrosoma hominis, 235
Python, 873
—— regius, 860
—— sebæ, 860

Q

Quarantine, in cholera, 396
Quartan fever, 27, 35, 36
—— —— parasite of, 27, 28, 33
Quartana duplex, 28
—— triplex, 28
Quinine amblyopia, 68
—— in diagnosis of malaria, 25, 62
—— in prophylaxis of malaria, 81
—— in puerperal state, 68
—— in treatment of malaria, 66
—— —— —— by intramuscular injection, 70
—— —— —— by intravenous injection, 73
—— —— —— by subcutaneous injection, 72
—— —— —— dosage of, 67
—— —— —— excretion of, 68
—— —— —— milk as menstruum for, 69
—— —— —— per os, 66
—— —— —— per rectum, 72
—— salts of, solubility and equivalent value of, 70 (footnote)
—— theory of blackwater fever, 102
Quotidian fever, 28

R

Rana nigromaculata, 817
"Rand scurvy," 377
Rashes of fevers in tropics, diagnosis of, 335
Rat, and infectious jaundice, 213
—— and plague, 256, 273
—— and rat-bite fever, 217
—— -leprosy, 508
—— post-mortem indications of plague in, 271 (footnote)
Rat-bite fever, 217

Digitized by Google

Rat-bite fever, definition of, 217
—— —— differential diagnosis of, 218
—— —— etiology of, 217
—— —— geographical distribution of, 217
—— —— history of, 217
—— —— pathology of, 218
—— —— symptoms of, 218
—— —— treatment of, 218
Rat-flea, bionomics of, 263
—— and plague, 260
Rat-mite, 775
Rats, plague species of, described, 276
Rattlesnakes, 684, 687
—— bites of, 687
Rattus alexandrinus, 813
—— —— and rat-bite fever, 218
—— decumanus, 759, 813
—— norvegicus, 759, 812
—— —— and Leptospira icterohæmorrhagiæ, 211
—— —— and plague, 257, 273
—— —— and rat-bite fever, 217
—— —— characters of, 277
—— rattus, 277, 759, 812, 813
—— —— and Leptospira icterohæmorrhagiæ, 211
—— —— and plague, 257, 273
—— —— and rat-bite fever, 218
—— —— characters of, 277
—— —— frugivorus, 277
—— —— rufescens, 277, 759, 855
Ray fungus, 709
Rectitis, epidemic gangrenous, 429
Rediæ, 785
Reduviidæ, 869
Relapsing bacillary dysentery, 413
—— fever, 170
—— —— definition of, 170
—— —— diagnosis of, 183
—— —— etiology of, 171
—— —— fulminating cases of, 182
—— —— geographical distribution of, 170
—— —— history of, 170
—— —— immunity from, 177
—— —— incubation period of, 178
—— —— morbid anatomy of, 183
—— —— mortality of, 183
—— —— parasites of, 171
—— —— —— cultivation of, 173
—— —— —— demonstration of, 172
—— —— —— different strains of, 173, 175
—— —— prophylaxis of, 185
—— —— symptoms of, 178, 181, 182
—— —— transmission of, 174
—— —— treatment of, 178
—— —— —— by arseno-benzol compounds, 184
—— —— —— by atoxyl, 185
—— —— —— by serum, 178
Remittent fever, malarial, 33
—— —— non-malarial, 314
—— pyrexia, prolonged (Cairo), 314
Reptilia, 872
Residual agglutinins, 901
—— bodies of malaria parasites, 19
Reynier's white mycetoma, 711
Rhabdonema intestinale, 847
Rhinosporidium seeberi, 781
Rhipicentor, 858
Rhipicephalus, 858
—— appendiculatus, 187
—— bursa, 187
—— evertsi, 187
—— sanguineus, 139, 776, 780
—— simus, 187
Rhizopoda, 749
Rhodnius prolixus, 138, 139
Rice, polished, and beriberi, 349
Rickettsia bodies, and spotted fever of Rocky Mountains, 235, 238
—— —— and trench fever, 247
—— prowazekii, 246
Robertson, Miss M., and glossina, 119, 120
Rockefeller Commission, on prophylaxis of ankylostomiasis, 675
—— —— on treatment of ankylostomiasis, 672, 673
Rocky Mountain fever (*see* Spotted fever)
Rogers, Sir Leonard, and amœbic dysentery, 442
—— —— and cholera, 400
—— —— and kala-azar, 148, 155, 157, 158
—— —— and leprosy, 523
Rosette body, 37
Ross's black spores, 58
—— researches in mosquito-malaria theory, 11
—— thick-film staining method, 879
Rubella, rash of, diagnosis of, 336
Russell's viper, 686
Russo's methylene-blue reaction, 908
Rynchobdella, 852

S

Sabethini, 91
Saccobranchus fossilis, 690
Sahib's disease, 147
Salek, 160
Salembini's anticholera serum, 403
"Salisbury cure," 486
Salvarsan compounds in amœbic dysentery, 444
—— —— in pellagra, 375
—— —— in rat-bite disease, 218
—— —— in relapsing fever, 184
—— —— in trypanosomiasis of man, 130 (footnote)
—— —— in verruga Peruviana, 547
—— —— in yaws, 539
—— —— methods of administering, 184
Sand-flea, 725
Sand-flies, differentiation of, from mosquitoes, 90
Sand-fly, and phlebotomus fever, 230
Saprospira, 783
—— grandis, 783
Sarcocystis muris, 781
—— tenella, 781
Sarcodina, 748, 749
Sarcophaga carnaria, 865 (Fig. 361)
Sarcopsyllidæ, 869, 870
Sarcoptes scabiei, 854
—— —— var. cameli, 854
Sarcoptidæ, 853, 854
Sarcosporidia, 781
Scabies, prevention and treatment of, 854
Scarlatina rheumatica, 221
Scarlet fever, rash of, diagnosis of, 335
Scaurus striatus, 814
Schaudinn's method of staining protozoa in fæces, 906
Schistosoma bovis, 558 (footnote), 801
—— cattoi (*see* Schistosoma japonicum)
—— hæmatobium, 556
—— —— cercaria stage of, 557
—— —— characters of, 554, 798

Digitized by Google

Schistosoma hæmatobium, free embryo of, 556
—— —— in dysentery, 468
—— —— life-history of, 557
—— —— miracidium of, 556
—— —— —— development of, in fresh-water snails, 557
—— —— ova of, 555, 558
—— —— sporocysts of, 557
—— japonicum, 570, 575
—— —— cercariæ of, 577, 580
—— —— characters of, 576, 801
—— —— miracidium of, 577
—— —— —— development of, 577
—— —— ova of, 577
—— —— sporocysts of, 578
—— mansoni, 556, 557, 558, 559, 560, 570
—— spindale, 801
Schistosomatidæ, 798
Schistosome eggs in urine, 909
Schistosomes, human, differential table of, 800
Schistosomiasis, 553
—— intestinal, 569
—— —— complement-deviation in, 573
—— —— definition of, 569
—— —— diagnosis of, 573
—— —— etiology of, 571
—— —— history and geographical distribution of, 569
—— —— prevention of, 575
—— —— prognosis of, 574
—— —— sigmoidoscopic examination in, 573
—— —— symptoms of, 571
—— —— treatment of, 574
—— mixed infestations in, 561
—— of the Far East, 575
—— —— —— definition of, 575
—— —— —— diagnosis of, 579
—— —— —— etiology of (*see* Schistosoma japonicum)
—— —— —— history and geographical distribution of, 575
—— —— —— morbid anatomy of, 578
—— —— —— prevention of, 580
—— —— —— symptoms of, 578
—— —— —— treatment of, 580
—— urinary, 553
—— —— cystoscopic examination in, 565
—— —— definition of, 553
—— —— diagnosis of, 564
—— —— Fairley's reaction in, 565
—— —— history and geographical distribution of, 553
—— —— parasite of (*see* Schistosoma hæmatobium)
—— —— pathological anatomy of, 562
—— —— prevention of, 568
—— —— prognosis of, 566
—— —— symptoms of, 560
—— —— treatment of, 566
Schizogony, 19
Schizogregarinæ, 771
Schizonts, 19
Schizotrypanum, 757
—— cruzi, 112, 764
Schüffner's dots, 36
Scolopendra cingulata, 872
—— morsitans, 692
Scopolamine, 680
Scorpæna, 690
Scorpionida, characters of, 862
Scorpions, stings of, 690
Screwworm infestation, 729
Scrotal elephantiasis, 621
Scurvy (in the tropics), 377
—— diagnosis of, 378
Scurvy, etiology of, 377
—— prophylaxis of, 379
—— Rand, 377
—— symptoms of, 377
—— treatment of, 378
—— vitamines and, 351, 352, 377
Septic sore (*see* Veld sore)
Septicæmic plague, 268
Serum-therapy in bacillary dysentery, 424
—— in cholera, 403
—— in infectious jaundice, 216
—— in plague, 276
—— in relapsing fever, 185
—— in snake-bite, 688
—— in undulant fever, 289
—— in veld sore, 701
—— in yellow fever, 205
Sesarma dehaani, 795
Seven-day fever, 219
—— —— etiology of, 220
—— —— geographical distribution of, 219
—— —— history of, 219
—— —— symptoms of, 219
Shiga-Kruse bacillus (*see* Bacillus dysenteriæ Shiga)
Shimamushi, 241
Ship beriberi, 347
Siderosis in malarial cachexia, 55
Simaruba bark in amœbic dysentery, 445
"Simple continued fever," 219, 314
Simulium midges, and pellagra, 368
—— reptans, 866 (Fig. 368)
Siphonaptera, characters of, 869
Sirkari disease, 147
Sitatunga, 763
Skin diseases, bacterial, 696
—— —— fungous, 705
—— —— non-specific, 693
—— —— of animal origin, 725
Sleeping sickness, discovery of cause of, 112
—— —— (*see also* Trypanosomiasis)
Slides, cleaning, 878
Smallpox, rash of, 335
Snake-bite, 684
—— colubrine, symptoms of, 686
—— treatment of, 687
—— —— serum-, 688
—— viperine, symptoms of, 686
Snake poisons, 684
Snakes, classification of, 872
—— synopsis of, 874
Soaps in fæces, 904
Sodium gynocardate in leprosy, 523
—— morrhuate, in leprosy, 523
Sodoku, 217
Sokiosa, 217
Sore feet of coolies, 676
Souma, 763
Spalax, 781
Sparganosis, ocular, 818
Sparganum mansoni, 817
—— proliferum, 818
Spectroscopic examination of urine, etc., 909
Spermophilus guttatus, 259
Spiders, 862
—— stings of, 691
Spirilla, 783
Spirillum fever, 170
Spirochæta, 782
—— gallinarum, 187
—— (*see also* Spironema)
Spirochætes, detection of, 910
—— in tissues, Levaditi's method of demonstrating, 923

Digitized by Google

Spirochætes, schema of different forms of, 212 (Fig. 65)
Spirochætosis, bronchial, 189
—— icterhæmorrhagica (*see* Infectious jaundice)
—— of fowls and geese, 783
Spironema, 783
—— anserinum, 783
—— berberum, 174, 175, 783
—— bronchiale, 189
—— buccale, 189, 783
—— carteri, 174, 175
—— cultivation of, 173
—— duttoni, 174, 175, 783
—— eugyratum (Fantham), 471, 783
—— —— in stools, 471
—— gallinarum, 783
—— novyi, 174, 175, 783
—— obermeieri (*see* Spironema recurrentis)
—— pallidum, 783
—— pertenue, 526, 783
—— —— and S. pallidum, 528
—— —— cultivation of, 528
—— —— demonstration of, 527
—— —— morphology of, 528
—— recurrentis, 171, 175, 212 (Fig. 65), 783
—— —— animal experiments with, 171
—— —— characters of, 171
—— —— demonstration of, 172
—— —— different stains of, 173
—— refringens, 783
—— schaudinni, 696
Spironemata, detection of, 910
Spleen, amœbic abscess of, 466
—— in malaria, 50, 54
Splenic anæmia (*see* Egyptian splenomegaly)
—— enlargement, in blackwater fever, 106
—— —— in enteric fever, 301
—— —— in infectious jaundice, 214
—— —— in malarial cachexia, 54
—— —— —— —— treatment of, 76
—— —— in relapsing fever, 179, 182, 183
—— —— in spotted fever of the Rocky Mountains, 237
—— —— in trypanosomiasis, 124
—— index in malarial cachexia, 54
—— rupture in malarial cachexia, 54
Splenomegaly, Egyptian (*see* Egyptian splenomegaly)
—— simple (*see* Egyptian splenomegaly)
Sporoblasts, 748
Sporocysts, daughter, 785
Sporogony, 20, 748
Sporotrichosis, 714
Sporotrichum beurmanni, 714
Sporozoa, 749, 770
Sporozoites, 19, 20
Spotted fever (of the Rocky Mountains), 235
—— —— complications of, 237
—— —— definition of, 235
—— —— diagnosis of, 239
—— —— —— —— of rash of, 336
—— —— etiology of, 238
—— —— geographical distribution of, 235
—— —— history of, 235
—— —— pathology of, 239
—— —— prophylaxis of, 239
—— —— symptoms of, 236
—— —— treatment of, 239
Sprue, 473
—— course of, 478
Sprue, definition of, 473
—— diagnosis of, 482
—— diarrhœa in, 477
—— dyspepsia in, 477
—— etiology of, 474
—— geographical distribution of, 475
—— incomplete, 479
—— —— gastric cases of, 479
—— —— intestinal cases of, 479
—— —— mouth cases of, 479
—— —— without diarrhœa, 479
—— intestinal atrophy consequent on, 479
—— morbid anatomy of, 480
—— nomenclature of, 473
—— pathology of, 481
—— prognosis of, 483
—— protopathic, 478
—— secondary to acute entero-colitis, 479
—— —— to dysentery, 478
—— symptoms of, 475
—— terminations of, 478
—— threatened relapses in, 484
—— treatment of, 483
—— —— by drugs, 488
—— —— by fruit, 485
—— —— by meat juice and underdone meat, 486
—— —— by milk, 483
—— —— by nutrient enemata or suppositories, 487
—— —— by vaccine, 488
—— —— climatic, 487
—— —— general, 487
—— types of, 478
"Squatting test" in beriberi, 356
Staining (*see* Blood-films)
Stains, formulæ of, 928
—— for paraffin sections, 929
—— solubilities of commoner, 930
Staphylococcus pyogenes albus, 701
—— —— aureus, 701
—— —— —— in craw-craw, 739
Stegomyia, 209
—— africana, 210
—— argenta punctata, 210
—— calopus, 776
—— fasciata, 776
—— —— and dengue, 223
—— —— and yellow fever, 195, 210
—— —— Lankesteria culicis in, 771
—— pseudoscutellaris, and filariasis, 590
—— scutellaris, 210
—— —— and dengue, 223
Sterigmatocystis nidulans, 710
Sternberg's mixture, composition of, 205
—— —— in blackwater fever, 109
—— —— in yellow fever, 205
Stomoxydinæ, 144
Stomoxys, 143, 144, 637
—— calcitrans, 634, 762, 866 (Fig. 366)
—— nebulosa, 762
—— nigra, 760
Strepsiceros capensis, 761
Streptococcus pyogenes, 701
—— salivarius vaccine in sprue, 488
—— viridans vaccine in sprue, 488
Strongylidæ, characters of, 821
Strongyloides, 735
—— intestinalis, and sprue, 474
—— stercoralis, 847
—— —— characters of, 848
—— —— larval forms of, 849
—— —— ova of, 848
Strongylus duodenalis, 829

Digitized by Google

Strongylus renalis, 825
—— siamense, 846
—— subtilis, 825
Strophanthus, 679
Strychnos, as source of arrow poisons, 680
—— tieuté, 679
Subintrant fevers, malarial, 32
Subtertian malarial fever, 39
—— —— —— clinical forms of, 42
—— —— —— geographical distribution of, 41
—— —— parasite, 27, 38
Succinea amphibia, 785
Sugar media, preparation of, 891
"Sun disease," 367
Sun-stroke (*see* Sun-traumatism)
Sun-traumatism, 323
—— morbid anatomy of, 323
—— pathogenesis of, 324
—— treatment of, 324
Superbin, 680
Surra, 111, 134, 760
Synanceia, 689
Syncopal subtertian malaria, 46
Syngamus dispar, 832
—— kingi, 832
Synkaryon, 772
Synovitis, filarial, 617
Syphacea obvelata, 824
Syphilis, diagnosis of yaws from, 538
Syringomyelia, diagnosis of leprosy from, 510

T

Tabanidæ, 760
Tabanus ustus, 760, 865 (Fig. 362)
Tænia africana, 809
—— caninum, 815
—— cucumerina, 815
—— cucurbitina, 807, 808
—— demerariensis, 814
—— dentata, 507
—— echinococcus, 809
—— —— brood-capsules of, 810
—— —— characters of, 809
—— —— cysts of, 810
—— —— diagnosis of, 811
—— —— geographical distribution of, 809
—— —— life-history and pathogenesis of, 810
—— elliptica, 815
—— flavopunctata, 813
—— hirudinacea, 850
—— hominis, 809
—— inermis, 808
—— lata, 808
—— leptocephala, 813
—— madagascariensis, 814
—— mediocanellata, 808
—— minima, 813
—— moniliformis, 815
—— nana, 811
—— pellucida, 807
—— philippina, 809
—— rhinaria, 859
—— saginata, 808
—— —— characters of, 808
—— —— geographical distribution of, 808
—— —— life-history and pathogenesis of, 809
—— —— ova of, in fæces, 655
—— —— varieties of, 809
Tænia solium, 807, 808
—— —— characters of, 807
—— —— geographical distribution of, 807
—— —— life-history and pathogenesis of, 808
—— —— ova of, in fæces, 655
—— tenella, 807
—— vulgaris, 807
Tæniidæ, characters of, 806
Tæniorhynchus fuscopennatus, 843
Tallequist's blotting-paper test, 888
Talma-Morison operation in Egyptian splenomegaly, 500
Tapeworms (*see* Cestodes)
Tarantula spider, 692
Taraxtogenos kurzii, 522
Tarbadillo (*see* Typhus fever)
Tarbagan, and plague, 259
Tarsonemidæ, 855
Tartar emetic (*see* Antimony)
Ternek, 679
Ternidens deminutus, 828
Tertian fever, 32, 38
—— —— parasite of, 27, 36
Tertiana duplex, 28
Tetramitidæ, 768
Tetramitus mesnili, 769
Tetratrichomonas, 769
Thalassophryne, 690
Thanatophidia 873
Theileria, 779
—— parva, 187, 542, 779, 780
Thelazia callipœda, 841
Thevetia ahonai, 680
—— neriifolia, 680
Thevetin, 680
Thevetosin, 680
Thoma-Zeiss hæmocytometer, 887
Thomson's serum agar, preparation of, 892
"Three-coloured worm," 847
Tick fever (*see* Relapsing fever)
—— paralysis, 239 (footnote)
Ticks, 186
—— generic classification of, 858
Tiger snake, 684
Timboin, 680
Tincta tincta, 792
Tinea cruris (*see* Dhobie's itch)
—— imbricata, 718
—— —— diagnosis of, 720
—— —— fungus of, 719
—— —— geographical distribution of, 718
—— —— prophylaxis of, 720
—— —— symptoms of, 718
—— —— treatment of, 720
"Tiqui-tiqui," in beriberi, 358
Tissue, connective, in fæces, 904
Titration, method of, 889
Tocotrema yokagawa, 793
Toxoplasma, 778
Trachinus, 690
Tragelaphus scriptus sylvaticus, 761
—— spekei, 763
Transfusion in blackwater fever, 108
Trematodes, 784
—— anatomy of, key to terminology of, 788 (footnote)
—— characters of, 784
—— life-history of, 785
—— ova of, 655 (Fig. 181)
—— parasitic in man, 786
Triatoma (*see* Conorhinus)
Tribondeau's hæmatoxylin test, 883
Trichina spiralis, 833
Trichinella spiralis, 833

Digitized by Google

Trichinella spiralis, characters of, 834
—— —— diagnosis of, 835
—— —— geographical distribution of, 833
—— —— life-history and pathogenesis of, 834
Trichocephalus dispar, 832
—— hominis, 832
Trichodectis canis, 815
Trichomonas hominis, 768
—— in bacillary-dysentery stools, 417
—— intestinalis, 470
Trichonocardiasis, 724
Trichosporon giganteum, 723
Trichostrongylus instabilis, 825
Trichotrachelidæ, characters of, 821
Trichuris trichiura, 832
—— —— characters of, 832
—— —— geographical distribution of, 832
—— —— life-history and pathogenesis of, 833
—— —— ova of, in fæces, 654
Triodontophorus deminutus, 828
Trombicula akamushi, 855
Trombidiidæ, 855
Trombidium akamushi, 242, 855
—— holosericum, 855
"Tropical anæmia," 659
" —— diarrhœa " (*see* Sprue)
—— fevers, imperfectly differentiated, 314
—— liver, 492
—— —— causes of, 492
—— —— treatment of, 493
—— sloughing phagedæna, 696
—— —— —— definition of, 696
—— —— —— diagnosis of, 698
—— —— etiology of, 697
—— —— —— geographical distribution of, 696
—— —— —— symptoms of, 697
—— —— —— treatment of, 698
—— sore, 160
—— splenomegaly, 147
Trypagar, preparation of, 893
Trypanoplasma, 764
—— helicis, 764
Trypanosoma, 756, 766
—— brucei, 111, 118, 119, 135, 136, 761
—— capræ, 763
—— cazalboui, 763
—— congolese, 764
—— cruzi, 112, 139, 764, 869
—— cuniculi, 759
—— dimorphon, 757, 763
—— ditæniatus, 760
—— duttoni, 759
—— equinum, 756, 762
—— equiperdum, 762
—— evansi, 111, 135, 143, 760
—— gambiense, 112, 113, 118, 119, 120, 134, 135, 757, 759
—— granulosum, 756
—— hippicum, 760
—— ingens, 762
—— lewisi, 111, 143, 759
—— microti, 759
—— nanum, 764
—— nigeriense, 112, 123, 759
—— pecaudi, 763
—— pecorum, 764
—— rhodesiense, 112, 135
—— rotatorium, 756
—— rougeti, 762
—— similæ, 764
—— somaliense, 761
—— theileri, 762
Trypanosoma uniforme, 763
—— vivax, 143, 757, 763
Trypanosomes, 756
—— agglomeration of, 116
—— arsenic-fast strains of, 132
—— crithidia-like forms of, 114
—— granule-shedding of, 114
—— habitat of, 133
—— habits of, 132
—— pathogenic African, Bruce's classification of, 758
Trypanosomiasis (of man), 111
—— complement-deviation test in, 129
—— definition of, 111
—— diagnosis of, 128
—— duration of, 117, 122
—— effect of, on abortion-rate and infant-mortality-rate, 125
—— etiology of, 113
—— geographical distribution of, 112
—— history of, 111
—— immunization in, 132
—— incubation period of, 121
—— infection with, during coitus, 134
—— morbid anatomy of, 127
—— mortality of, 126
—— predisposing causes of, 121
—— prophylaxis of, 132
—— rôle of tse-tse fly in, 117
—— sleeping sickness stage of, 125
—— symptoms of, 122
—— (T. cruzi), 138
—— —— diagnosis of, 142
—— —— etiology of, 139
—— —— geographical distribution of, 138
—— —— history of, 138
—— —— pathological anatomy of, 142
—— —— prophylaxis of, 142
—— —— treatment of, 142
—— (T. rhodesiense), 135
—— —— etiology of, 135
—— —— prophylaxis of, 137
—— —— symptoms of, 137
—— —— treatment of, 137
—— treatment of, 129, 137
—— —— by antimony, 130
—— —— by arsenic, 129
—— —— by atoxyl, 130, 137
—— —— by salvarsan, 130 (footnote)
—— Wassermann reaction and, 128 (footnote)
Trypsin agar, preparation of, 892
Trypsinized broth, preparation of, 892
Tse-tse flies (*see* Glossina)
Tsutsugamushi, 241
Tuberculin in leprosy, 524
Tuberculous ulceration of bowel, 471
Tumbu fly, 732
Tunnel disease (*see* Ankylostomiasis)
Tuntun, 659
Typhlopidæ, 873
Typhoid fever (*see* Enteric fever)
—— remittent fever, 42
"Typho-malarial fever," 309
Typhus exanthemicus (*see* Typhus fever)
—— fever (in the tropics), 246
—— —— definition of, 246
—— —— diagnosis of, 249
—— —— etiology of, 246
—— —— morbid anatomy of, 247
—— —— prophylaxis of, 250
—— —— rash of, 335
—— —— symptoms of, 247
—— —— treatment of, 250
—— Weil-Felix reaction in, 249, 902
Tyroglyphidæ, 855
Tyroglyphus, 728

Digitized by Google

U

Ulcerating dematitis, 738
—— granuloma of pudenda, 548
—— —— —— definition of, 548
—— —— —— diagnosis of, 551
—— —— —— etiology of, 548
—— —— —— geographical distribution of, 548
—— —— —— histology of, 550
—— —— —— parasitic elements in, 548
—— —— —— spirochætes in, 548
—— —— —— symptoms of, 549
—— —— —— treatment of, 551
—— —— —— —— by tartar emetic, 552
Ulcerous rhino-pharyngitis, destructive, yaws and, 532
Ulcus tropicum (*see* Tropical sloughing phagedæna)
Uncinaria americana, 829
—— duodenalis, 829
Undulant fever, 278
—— —— age and, 280
—— —— agglutination in, 286, 902
—— —— complications of, 285
—— —— definition of, 278
—— —— diagnosis of, 286
—— —— duration of, 285
—— —— etiology of, 279
—— —— geographical distribution of, 278
—— —— goat's milk and, 282
—— —— history of, 279
—— —— immunity from, 282
—— —— incidence of, in Army and Navy, 279
—— —— incubation period of, 282
—— —— local causes of, 281
—— —— milk and, 282
—— —— mode of infection in, 281
—— —— morbid anatomy and pathology of, 285
—— —— mortality of, 285
—— —— paramelitensis group of cases of, 279, 286
—— —— prevention of, 289
—— —— prognosis of, 287
—— —— season and, 280
—— —— sequelæ of, 285
—— —— symptoms of, 283
—— —— treatment of, 287
—— —— —— by serum, 289
—— —— —— by vaccines, 288
Uragoya granatensis, 442
Urechites suberecta, 680
Urechitin, 680
Urechitoxin, 680
Urine, blood-corpuscles, red, in, 908
—— —— white, in, 908
—— casts in, 909
—— epithelial cells in, 909
—— examination of, in tropics, methods of, 908
—— —— spectroscopic, 909
—— organisms in, 908
—— —— cultivation of, 903
—— ova of schistosomes in, 909
—— pus-corpuscles in, 908
Urobilin test for urine, 908
Uta, 166

V

Vaccination, and communication of leprosy, 525
Vaccine-therapy in bacillary dysentery, 426
Vaccine-therapy in enteric fever, 309
—— in sprue, 488
—— in undulant fever, 288
Vacuoles, in blood-corpuscles, diagnosis of, 24
Van Gieson's picro-fuchsin stain, 930
Varices, lymphatic, cutaneous and deeper, 610
Varicose groin-glands, 608
—— —— —— diagnosis of, 609
—— —— —— pathological anatomy of, 609
—— —— —— symptoms of, 608
—— —— —— treatment of, 610
Vegetable poisons, 679
Veld sore, 699
—— —— definition of, 699
—— —— etiology of, 699
—— —— geographical distribution of, 699
—— —— prophylaxis of, 701
—— —— symptoms of, 699
—— —— treatment of, 701
Velvet mites, 855
Ver du Cayor, 732
—— macaque, 730
Verminous dysentery, 468
Verruga Peruviana, 544
—— —— definition of, 544
—— —— etiology of, 544
—— —— geographical distribution of, 544
—— —— pathology of, 545
—— —— symptoms of, 545
—— —— treatment of, 547
Vibrio, cholera (*see* Comma bacillus)
Vincent's white mycetoma, 709
Vipera russellii, 684
Viperidæ, 873, 874
—— synopsis of, 877
Viperinæ, 874
—— synopsis of, 877
Vitamines, and beriberi, 351
—— and pellagra, 369
Vitiligo, 695
—— diagnosis of leprosy from, 510
Volume to mass, relation of, 933
Vomiting sickness of Jamaica, 681

W

Wanganga, 607
Warburg's tincture, 74
War œdema (*see* Epidemic dropsy)
Waskia intestinalis, 769
Wassermann reaction in infectious jaundice, 215
—— —— in leishmaniasis Americana, 168
—— —— in leprosy, 510 (footnote)
—— —— in relapsing fever, 183
—— —— in yaws, 532
—— —— technique of, suitable for tropics, 913
Water itch, 675
—— pox, 675
—— sores, 576
Water-soluble B. 352
Watsonius watsoni, 803
—— —— characters of, 803
—— —— discovery of, 803
—— —— geographical distribution of, 803
—— —— life-history of, 803
—— —— treatment, 803
Weigert-Gram method of demonstrating fibrin and bacteria in sections, 923

Digitized by Google

Weigert's iron hæmatoxylin stain, 930
—— —— —— —— and van Gieson stain, 922
Weil-Felix reaction, 249, 902
Weil's disease (*see* Infectious jaundice)
"Wet beriberi," 346
Whip-worm, 832
Widal reaction, technique of, 897
—— —— (*see also* Agglutination)
Wildebeest, 761
Woodchuck, 238
Worms, preservation of, 784

X

X 19, 250
Xenopeylla, 870
—— cheopis, 260, 261, 760, 814
X-ray treatment of blastomycosis, 715
—— —— of oriental sore, 166
—— —— of ulcerating granuloma of pudenda, 551

Y

Yangona, 683
Yaws, 526
—— age and, 527
—— bone lesions in, 535
—— definition of, 526
—— diagnosis of, 538
—— duration and recurrences of, 534
—— eruption of, 529
—— etiology of, 527
—— gangosa and, 532
—— general health in, 536
—— geographical distribution of, 526
—— gland-enlargement in, 532
—— head and foot lesions in, 532
—— incubation period of, 528
—— morbid anatomy and pathology of, 538
—— mortality of, 537
—— place of origin of, 526
—— primary stage of, 528
—— prophylaxis of, 539
"—— ringworm," 531
—— secondary stage of, 529
—— sequelæ of, 536
—— spironema of, 526, 527
Yaws, spironema of, cultivation of, 528
—— symptoms of, 528
—— synovitis in, 536
—— tertiary stage of, 532
—— treatment of, 539
—— —— by salvarsan compounds, 539
Yeast theory of sprue, 474
Yellow fever, 190
—— —— black vomit in, 200
—— —— definition of, 190
—— —— diagnosis of, 203
—— —— —— of malaria from, 64
—— —— duration of infectiveness in, 193
—— —— epidemiology of, 191
—— —— etiology of, 193
—— —— geographical distribution of, 190
—— —— germ of, 193
—— —— immunity from, 192
—— —— —— of natives, 208
—— —— incubation period of, 192
—— —— mortality of, 201
—— —— non-infectiveness of fomites, etc., in, 207
—— —— pathological anatomy of, 202
—— —— period of calm in, 201
—— —— —— of reaction in, 201
—— —— possible introduction of, into Asia, 209
—— —— prognosis of, 201
—— —— prophylaxis of, 205
—— —— race and, 192
—— —— Stegomyia fasciata and, 195
—— —— symptoms of, 197
—— —— treatment of, 204
—— —— —— serum, 205
—— —— —— Sternberg's, 205
—— —— vaccination for, 208
Yemen ulcer, 696
Yokagawa yokagawa, 793

Z

Zappert slide, for enumeration of minute objects, 888
Zein, pellagra and, 370
Zeist theory of pellagra, 368
Ziehl-Neelsen carbol-fuchsin stain, 928
Zygotes, 19
Zygotoblasts, 20

PRINTED BY CASSELL & COMPANY, LIMITED, LA BELLE SAUVAGE, LONDON, E.C.4
40.121

Digitized by Google

Digitized by Google

LANE MEDICAL LIBRARY

This book should be returned on or before
the date last stamped below.

10M-4-49—63290

Digitized by Google

L961
M289
1921

Manson, Sir Patrick
Manson's tropical
diseases.

NAME	DATE DUE

10M-

Digitized by Google